SHORT-TERM SACCADIC ADAPTATION IN THE MACAQUE MONKEY: A BINOCULAR MECHANISM

K. P. Schultz and C. Busettini

Department of Vision Sciences
and
Vision Science Research Center
University of Alabama at Birmingham
Birmingham, AL 35294

Running Head:
SHORT-TERM SACCADIC ADAPTATION

Abstract: 250 words
Text pages: 67
Figures: 16
Tables: 0

Address correspondence to:
C. Busettini
Vision Science Research Center
612 Worrell Bldg.
924 18th St. South
Birmingham, AL 35294-4390
USA
Tel: 205-934-2601 Fax: 205-934-5725
e-mail: cbus@uab.edu
ABSTRACT

Saccadic eye movements are rapid transfers of gaze between objects of interest. Their duration is too short for the visual system to be able to follow their progress in time. Adaptive mechanisms constantly recalibrate the saccadic responses by detecting how close the landings are to the selected targets. The double-step saccadic paradigm is a common method to simulate alterations in saccadic gain. While the subject is responding to a first target shift, a second shift is introduced in the middle of this movement, which masks it from visual detection. The error in landing introduced by the second shift is interpreted by the brain as an error in the programming of the initial response, with gradual gain changes aimed at compensating the apparent sensorimotor mismatch. A second shift applied dichoptically to only one eye introduces disconjugate landing errors between the two eyes. A monocular adaptive system would independently modify only the gain of the eye exposed to the second shift in order to reestablish binocular alignment. Our results support a binocular mechanism. A version-based saccadic adaptive process detects postsaccadic version errors and generates compensatory conjugate gain alterations. A vergence-based saccadic adaptive process detects postsaccadic disparity errors and generates corrective non-visual disparity signals that are sent to the vergence system to regain binocularity. This results in striking dynamical similarities between visually-driven combined saccade-vergence gaze transfers, where the disparity is given by the visual targets, and the double-step adaptive disconjugate responses, where an adaptive disparity signal is generated internally by the saccadic system.
INTRODUCTION

Visually-driven transfers of gaze between stationary targets located at different eccentricities and depths are usually achieved by a combination of saccadic and vergence responses. When the required eccentricity and vergence changes are more than a few degrees, an initial smooth vergence response precedes the primary saccade and resumes after its end, with a brisk intrasaccadic acceleration of the rate of vergence change (Busettini and Mays 2005a; van Leeuwen et al. 1998; Collewijn et al. 1997, 1995; Maxwell and King 1992; Zee et al. 1992). One or more corrective saccades might follow, often with additional smooth vergence contributions between the corrective saccades. If the depth change between the two targets is gradually decreased relative to the change in cyclopean eccentricity, the onset of the presaccadic smooth vergence contribution is delayed (Busettini and Mays 2005a) and its amplitude becomes increasingly smaller, until the entire change in depth can sometimes be achieved inside the primary saccade with no evident pre or postsaccadic smooth components: pure asymmetric saccades (Enright 1992; Maxwell and King 1992). Real stimuli simulating natural environments were reported to be more efficient in generating asymmetric saccades than standard impoverished laboratory configurations (Erkelens et al. 1989a), with the intrasaccadic asymmetry of the primary saccade covering a much larger ratio of the overall change in depth.

A similar gradual transition from mixed vergence-saccadic responses to pure asymmetric saccades is seen during experiments in humans that use horizontal aniseikonic patterns. Both eyes see the same pattern but with different horizontal magnifications, giving the perception of a tilted plane in depth (Bucci et al. 1999; Bruno et al. 1995; Kapoula et al. 1995; Van der Steen and Bruno 1995). Decreasing the magnification ratio increases the probability of pure asymmetric saccades. Similar results were reported with anisometropic spectacles (Erkelens et al. 1989b). For monkeys, there is only one preliminary report by Bush et al. (1994), where it is described that, for a horizontal aniseikonic ratio of 10% between the right-eye and the left-eye images, the asymmetric saccades often
had no detectable presaccadic or postsaccadic vergence components. When the ratio was increased to 20%, extrasaccadic smooth vergence components were present in most trials, often starting before the primary saccade. The authors suggested that there is a limit to the achievable amount of monocular saccadic asymmetry, with the need for the recruitment of the slower (binocular) smooth vergence above a certain threshold.

Pure asymmetric saccades were often seen as clear evidence that the saccadic system is capable of generating independent (monocular) commands to the two eyes, directly challenging Hering’s law of equal innervation (Hering 1868). Nonetheless, the role of disparity/vergence signals in these saccades remains unclear. A true monocular saccadic system with independent right-eye and left-eye saccadic generators, each with its own adaptive gain element, would not need to use binocular mechanisms, with each eye responding and adapting to what it sees (ex. chameleon). On the contrary, it might be that activation of the vergence system is necessary, in primates, to generate disconjugate saccadic commands, with disparity- or vergence-related signals directly modulating the saccadic asymmetry. In fact, Busettini and Mays (2005b) found that, after the contribution of the smooth vergence component is subtracted, the amount of intrasaccadic asymmetry in the monkey during visually-driven combined saccade-vergence responses is related to the vergence motor error at the time of the saccade and not to the initial visual goal of the movement. A recent model (Erkelens 2011) simulated the intrasaccadic vergence enhancement as a multiplicative interaction between vergence velocity and saccadic burst signals.

Is it possible, in primates, to generate asymmetric saccades with no activation at all of the vergence system? In 3-D gaze transfers, from which most of the neural evidence for monocularly-driven saccades originates (for a review see Cullen and Van Horn 2011 and King 2011), the visual system presents to the oculomotor systems the needed change in eccentricity (cyclopean error) and the needed depth change (disparity error) before the start of the eye movement. Even small visual
disparity errors will likely activate the vergence system. In the aniseikonic case, asymmetric responses can be observed in the monkey in the very first trial (Bush et al. 1994), indicating the presence of a direct non-adaptive visually-driven process. In humans, an immediate response is followed by a gradual adaptive component (Bruno et al. 1995). The presence of smooth vergence responses, often preceding the primary saccade for an aniseikonic ratio as small as 20%, indicates that the vergence system is likely engaged, in some form, also during aniseikonic tasks.

Saccadic short-term adaptation to simulated disconjugate gain alterations between the two eyes is another paradigm that can be used to generate asymmetric saccades. In this case, the occurrence of the disconjugacy is causally linked to the occurrence of the saccade, with no prior visual disparity or aniseikonic information. Thus, the saccadic system is entirely in charge of generating the disconjugate adaptive response, making this design ideally suited to unmask a monocular mechanism, if present. To compare the metrics of visually-driven and adaptive oculomotor behavior in exactly identical conditions, we used the double-step saccadic paradigm (McLaughlin 1967; Hopp and Fuchs 2004 for a in-depth review). When a target that the animal is actively fixating with both eyes suddenly moves in a step-wise fashion (primary step) to a new location on the same isovergence circle, i.e., with no change in depth, the animal will produce a conjugate (i.e., identical rotations of the two eyes) saccadic eye movement to bring its eyes to the new target location. In the traditional conjugate double-step saccadic paradigm, while the animal is in the middle of the execution of the saccade elicited by the primary step, the target, continuously presented to both eyes, is stepped a second time (secondary step) to another location on the same isovergence circle. This generates an apparent conjugate sensorimotor mismatch between what the animal programmed on the basis of the target’s primary step and the total change in target position. By shifting the target during the saccade, when target motion is not perceived (Riggs et al. 1982; Brooks and Fuchs 1975), the brain interprets the landing error as a mistake in the programming of the primary saccade. Once the
landing error is visually detected, the animal will generate a conjugate corrective saccade to move its eyes to the shifted location. If the target is moved this way consistently over many trials, the gain of the primary saccade is adjusted by the animal to compensate for the repeated landing errors. For example, for a primary step of 10° and a secondary step of 2° forward, the animal, if perfect compensation is achieved, will execute 12° primary saccades, despite having only seen 10° target steps throughout the session. This change in saccadic gain remains for a period of time after the stimulus is returned to normal, i.e., with no further delivery of intrasaccadic secondary steps, indicating true adaptation (Hopp and Fuchs 2004; Albano 1996; Albano and Marrero 1995; Straube and Deubel 1995; Frens and van Opstal 1994; Albano and King 1989; Semmlow et al. 1989; Deubel et al. 1986; Miller et al. 1981; McLaughlin 1967). A significant part of this adaptation is achieved inside a single experimental session, and therefore it is referred to as a short-term adaptation. Interestingly, human conjugate adaptation reaches a steady-state level in less than 100 trials, while monkeys often need 1000 or more trials (Hopp and Fuchs 2004; Straube et al. 1997a). In a similar fashion, if the secondary step is applied to only one eye using a dichoptic arrangement – both eyes see the initial conjugate primary step and have uninterrupted view of their respective targets throughout the trial, but there is no secondary step on the other eye - a disconjugate (i.e., different in the two eyes) adaptation can occur (Kapoula et al. 1996; Eggert and Kapoula 1995; Albano and Marrero 1995). We are not aware of studies where disconjugate double-step saccadic paradigms were tested in macaque monkeys. The key difference with respect to the standard conjugate paradigm is that disconjugate secondary steps introduce a visual disparity. Thus, prior to adaptation, the visual disconjugacy of the landing error is mostly dealt with by a smooth vergence response, i.e., by a non-saccadic response. How this postsaccadic visual disparity is converted into a saccadic-generated adaptive response is still unresolved. Does a monocular saccadic recalibration independently adjust the gain of each eye? Does the saccadic system generate an internal model of this postsaccadic
disparity error, which is then fed to the vergence system? In the latter hypothesis, which is the focus of this work, we expect to see evident similarities in the oculomotor responses between disconjugate controls, where the secondary steps are included into the primary steps to obtain standard single-step disconjugate visual stimuli, and disconjugate adaptive responses. In this binocular mechanism, the visual disparity error is simply replaced by a saccadic-generated adaptive disparity error. In a monocular adaptation mechanism, the adaptation to disconjugate secondary steps will be very similar, in time course and dynamic characteristics, to the adaptation to identical secondary steps in the two eyes, with each eye separately adjusting its gain independently of what is applied to the other eye.

We will analyze macaque saccadic adaptation to bi-ocular (identical secondary steps applied to the two eyes), uni-ocular (secondary step applied to only one eye), and symmetric (equal and opposite secondary steps applied to the two eyes) paradigms. We used these unconventional names for the paradigms to reserve the terms conjugate, monocular, and binocular to the underlying neural mechanisms being tested.

METHODS

Binocular horizontal and vertical eye movements were recorded in two rhesus monkeys (Macaca mulatta), weighing 6-10 Kg, while performing saccadic visually-driven controls or adaptive paradigms. The data presented here were acquired from intact animals before the implantation of chambers for single unit recordings. All procedures and experimental protocols were approved by UAB Institutional Animal Care and Use Committee, and complied with USDA, AAALAC, and U.S. Public Health Service Policy on the humane care and use of laboratory animals.

Surgical procedures

After being trained to enter a primate chair and being acclimated to the lab environment, a series of aseptic surgical procedures were performed on the animals. Custom-made PEEK strips were
attached to the skull with ceramic bone screws. After full recovery, the strips were used as attachments for an external head post. Coils were implanted underneath the conjunctiva of the right and left eyes for the purpose of binocular eye tracking via the magnetic search coil technique (Fuchs and Robinson 1966).

Behavioral paradigms

Animals were trained to make saccades and vergence responses between visual targets presented dichoptically to the two eyes for a reward while their heads were immobilized. The dichoptic arrangement was obtained using matching orthogonal polarizers and a non-depolarizing back-projection screen. The screen was placed at 410 mm from the animal’s corneal apex, equivalent, for the two animals when looking straight ahead, to a vergence angle of 4.4°. With the exclusion of the targets, the room was carefully darkened. The 1° targets were polarized images of bright red LEDs remotely projected by 100 mm lenses onto the non-depolarizing screen, and their position was controlled by mirror galvanometers (GSI Lumonics®) in an x-y configuration. The four galvanometers were driven by 1 kHz analog signals generated by the 16-bit D/A converters of the laboratory computer, running a custom package under a real-time Ubuntu kernel. The same computer monitored the animal behavior, timed the stimuli, administered rewards, and acquired, also at 1 kHz with 16-bit A/D resolution, the eye position signals, the feedback signals from the galvanometers, and the signals driving the LEDs. Horizontal and vertical eye position and mirror signals were analogically filtered with anti-aliasing 200 Hz low pass 48dB/octave Bessel filters prior to acquisition.

The study included 6 main double-step saccadic paradigms, which are described in the top and middle panels in Fig. 1. In all experiments the targets remained on the horizontal meridian, with only horizontal shifts. (FIGURE 1 NEAR HERE) The primary steps were always identical in the two eyes in all paradigms, and therefore the resulting binocular percept moved in space along isovergence circles. The sizes of the secondary steps were 20% (forward or backward) of the sizes of the primary
steps in the bi-ocular (BC, BA) and uni-ocular (UC, UA) cases, and 10% (forward in one eye, backward in the other eye) in the symmetric (SC, SA) cases (see also Robinson et al. 2003). As illustrated in Fig. 1, the difference between the visual controls (top row) and the correspondent adaptive paradigms (middle row) was in the time of delivery of the secondary steps. In the controls, the secondary steps were added on top of the primary steps, which, in Fig. 1, were rightward 10° steps. The delivery of the secondary steps during the adaptive sessions was experimentally set to occur around the peak velocity of the primary saccade. Trials with spurious triggering of the secondary steps, detected by comparing the eye traces with the mirror feedback traces, were manually rejected during the off-line analysis. In the adaptive trials, the LEDs were briefly turned off for 5 ms during the <4 ms movement of the mirrors associated with the secondary steps to even further reduce the possibility for the animal to detect motion. For consistency, the LEDs were also turned off at the same time inside the primary saccade in the control paradigms, even if no secondary steps were delivered at that time.

With the exclusion of the symmetric experiments (SC and SA), which were done only in the fully-predictive paradigm (see below), all the other experiments were done in two configurations. In the fully-predictive paradigm, rightward 10° primary target steps were always followed by leftward 10°, followed again by rightward 10°, and so on, until the end of the session. This paradigm is illustrated in the bottom left panel in Fig. 1, reporting the uni-ocular case with +20% secondary steps applied only on the right eye. Rightward and upward eye movements are reported as positive, while leftward and downward movements are reported as negative. With (horizontal) vergence (VG) defined as $H_L - H_R$, crossed disparities and convergence are reported as positive values, and uncrossed disparities and divergence as negative. Starting from point A (cyclopean angle 5.5°, vergence angle 7.4°), which is the endpoint of the rightward trials in this example, the leftward 10° conjugate primary step is applied, with the binocular percept traveling along the 7.4° isovergence circle. At the end of the
primary step, point A\textsubscript{P} is at a cyclopean angle of -4.5\(^\circ\). The 2\(^\circ\) leftward secondary step, applied only to the right eye, causes the binocular percept to move onto the 9.4\(^\circ\) isovergence circle and to a cyclopean angle of -5.5\(^\circ\) (point B), which is the endpoint of the leftward trials. The next sequence, with a rightward 10\(^\circ\) conjugate primary step and a 2\(^\circ\) rightward secondary step, again applied only to the right eye, brings the binocular percept back to A. The right-eye mirror and left-eye mirror were calibrated separately with non-linear look-up tables to obtain these trajectories in space. Thus, the animal knew exactly what was going to happen throughout the session after a few trials, both in the control and in the adaptive cases. This fully-predictive design (A\(\rightarrow\)B\(\rightarrow\)A\(\rightarrow\)B and so on), obviously artificial, was adopted with the expectation that it would maximize the probability of eliciting pure asymmetric saccades and, in the adaptive paradigm, the speed of the adaptive process. In the pseudo-random design (bottom right panel), the primary target steps, still always horizontal and identical in the two eyes, were right 5\(^\circ\), right 10\(^\circ\), left 5\(^\circ\), or left 10\(^\circ\), pseudo-randomly intermixed. Thus, the sequence of ending points (also starting points for the subsequent trial, as before) followed a non-predictable trajectory in both vergence and eccentricity (in the figure, A to F as example). At each starting position, any of the 4 primary steps could be randomly selected, with the only limitation for the targets to remain inside a horizontal version range of ±25\(^\circ\), and between 4.4\(^\circ\) and 12.4\(^\circ\) of convergence angle. This forcibly limited the selection of the next primary step when the animal was near the edges of the version and the vergence ranges, and thus the “pseudo-random” term used for this paradigm. The trial lists for the pseudo-random paradigms were computed offline, with the weights of the random generator adjusted to have an approximately balanced number of 5\(^\circ\) and 10\(^\circ\) primary steps. Without this correction, due to the imposed target positional limits, the 10\(^\circ\) steps had a higher probability of getting rejected because of a higher probability of stepping out of the oculomotor boundaries. This second design was adopted because it more closely resembles what the animal would experience during natural scene scanning while having an altered saccadic gain, and to
have an estimate of the influence of prediction in the adaptive process. Although both designs have been used before, this is the first study to compare the two. In both designs, the vergence steps were balanced with respect to the isovergence circle at 8.4°. In pilot experiments, the vergence steps were balanced with respect to the isovergence circle at 4.4°, i.e., to the circle tangent to the screen, in order to minimize the amount of vergence-accommodation dissociation, but during the control sessions both animals had difficulties in diverging beyond the screen, while they had no difficulties in converging to 12.4°. With both control and adaptive cases having identical geometrical configurations, we considered it likely that any effects on the responses linked to the vergence-accommodation dissociation would be similar for both paradigms. Thus, we rebalanced the paradigms with respect to the 8.4° isovergence circle, which also became the locus of the targets in the bi-ocular paradigms.

The behavioral task required of the animal for a juice reward was limited to responding to the primary steps. The targets defining the primary steps were presented in sequence with no delay or overlap between them. The animal had 2000 ms to acquire each target. As soon as its eyes were inside the eye position windows associated with the current target, a required fixation period started (a fixed period of 1000 ms in the fully-predictive design, and a random period between 800-1200 ms in the pseudo-random design). In the aborted trials, i.e., when the animal’s eyes did not enter inside the required positional windows in the allotted time or exited from them too early by breaking fixation, the LEDs were immediately turned off as soon as the animal’s error was detected and remained off for 3000 ms, when the next trial in the trial sequence started, to try to minimize the impact of the animal’s errors on the adaptive process. The sizes of the computer eye position windows inside which the animal had to bring its eyes and remain inside to receive a reward were ±4°, and were only used to detect that the animal was actively performing the primary saccades.

The list of possible experiments that could be obtained from the two designs was limited by the fact that, for example, in the fully-predictive design if the rightward saccades were associated with
a convergence secondary step, the leftward saccades had to be associated with a divergence secondary step. Each of the two animals performed a total of 31 different experiments. Mainly interested in a direct comparison between the fully-predictive and the pseudo-random paradigms, we analyzed only the $10^\circ$ pseudo-random data, taking into account that the $10^\circ$ trials occurred, in this design, only 50% of the time.

After 60 eye calibration trials using a rigid board with embedded horizontal and vertical non-polarized LED targets, the calibration board was replaced with the non-depolarizing screen. In preliminary sessions we tested, in both animals, if there were significant differences between a monocular calibration, in which each eye’s data were acquired separately while the other eye was patched, or a single binocular calibration with both eyes viewing. When no differences in the calibration functions were apparent, we decided to use a binocular calibration on both animals to minimize the number of calibration trials. One hundred $10^\circ$ primary-only saccades (50 rightward, 50 leftward) were then acquired in all sessions, control or adaptive, as baseline. The actual experiment then started. The randomly selected control or adaptive experiment assigned to the session of the day continued until the animal lost interest in the task and the animal was returned to its home cage.

Data analysis

Horizontal (H) and vertical (V) eye position traces were linearized with 3rd-order polynomials in both horizontal and vertical coefficients, determined with the calibration board, to compensate for possible coil and phase detector horizontal/vertical cross-talks, and fit with a cubic spline. Velocity signals ($H', V'$) were then calculated using a 2-point backward differentiation. The primary saccades were manually identified, and the 2-segments fitting process outlined in Busettini and Mays (2005a) was applied to identify the quadrant saccadic onset ($S_{ON}$) and offset ($S_{OFF}$). Once the onset and offset of the primary saccade was determined, all traces were synchronized with respect to saccadic onset or offset, depending on the aspect being addressed.
For the analysis, each trial was divided into four main time segments. The presaccadic (PR) segment started at the onset of the primary target steps and ended at the onset of the primary saccade. The intrasaccadic (IN) segment started at the onset and ended at the offset of the primary saccade. The immediate postsaccadic (PO\textsubscript{[0-50]}) segment started at the offset of the primary saccade and ended 50 ms after the offset. These three segments together defined the PREVISUAL interval. All the response components starting 50 ms after the offset of the primary saccade were defined as VISUAL. Each of these time periods involves specific neural events, which will be briefly discussed here. Busettini and Mays (2003) have shown that, during combined vergence-saccadic responses, macaque brainstem saccadic omnipause neurons (OPNs) pause only during the intrasaccadic (IN) periods, and are at or near baseline firing elsewhere. Furthermore, the timings of the onset and offset of the OPN saccadic-related pause, for both saccades alone and when associated with an ongoing vergence, were found to be very similar, and tightly linked to the onset and offset of the version component of the saccadic response. Similarly, Missal and Keller (2002) have reported that some OPNs slow their firing during conjugate smooth pursuit, but, as observed for vergence, they stopped their firing only in correspondence to the catch-up saccades. When the OPNs are firing at or near baseline, the inhibition of the short-lead saccadic burst neurons by the OPNs blocks any saccadic command from reaching the motoneurons of the extraocular muscles (Keller et al. 1996; Scudder 1988), necessarily implying that, in the monkey, any smooth response outside the actual saccades has no active contributions from the saccadic system. This is also confirmed by direct recordings of short-lead burst neurons during similar visual vergence-saccadic tasks (Van Horn et al. 2008). (ENDNOTE 1 AT BOTTOM OF THIS PAGE) Excluding corrective saccades or saccadic intrusions, this means that the saccadic system is active at the level of the short-lead burst neurons only during the IN time period. Of interest for our study will be the presence of smooth version or vergence responses during the PR time period, indicating that their onset can precede the onset of the primary saccade. The selection of 50 ms for the
duration of the $\text{PO}_{[0-50]}$ time period derived from the latency values reported in the literature for the visually-driven ultra-short latency version (Miles et al. 1986; Kawano and Miles 1986; Busettoni et al. 1991) and vergence (Busettini et al. 1996) responses in the monkey. The 50 ms value guaranteed that no part of the responses observed in the $\text{PO}_{[0-50]}$ period was elicited by postsaccadic visual feedback. As a consequence, any response after the $\text{PO}_{[0-50]}$ period was defined as potentially visually-driven: VISUAL segment. $\text{VIS}_{[0-100]}$ was defined as the first 100 ms time period of the VISUAL segment, and $\text{VIS}_{[100-200]}$ was defined as the next 100 ms interval. The extended postsaccadic interval $\text{PO}_{[0-600]}$ was defined as the interval between the end of the primary saccade and 600 ms after this event. With our definition of VISUAL, $\text{PO}_{[0-600]}$ included 550 ms of potential visual contributions.

All version, vergence, right-eye, and left-eye measures reported in this paper are horizontal measures. Responses contaminated by vertical movements were rejected during the initial visual inspection. All reported statistical significances are at the $P<0.01$ level, and the $R^2$ are mean corrected.

RESULTS

This section is structured into three main segments. The first illustrates the results associated with the bi-ocular paradigm in the fully-predictive design, with particular focus on the adaptive constants, the conjugacy of the adaptive responses, and the nature of the postsaccadic drifts. The second section describes the results associated with the uni-ocular and symmetric paradigms, also in the fully-predictive design. Of particular importance is a comparison of their adaptive constants and postsaccadic behavior with the bi-ocular case. Finally, the third section briefly reports the main results obtained with the pseudo-random design and how they compare with the fully-predictive design to look for any influence of prediction in the conjugate and disconjugate short-term adaptive process.

*Fully-predictive design bi-ocular paradigms*
ADAPTIVE CONSTANTS AND CONJUGACY. Two fully-predictive bi-ocular adaptive experiments (BA in Fig. 1) and associated controls (BC in Fig. 1) were performed with each animal. In the first adaptive experiment, a $2^\circ$ forward secondary step was applied during both rightward and leftward $10^\circ$ primary saccades, which simulated a sudden 20% bidirectional reduction in saccadic gain by causing the animal to consistently undershoot the target. As shown in Fig. 2A (animal #1, rightward saccades), the animal reacted to the repeated undershoots by increasing the intrasaccadic version position change of the primary saccade. In the second experiment, a $2^\circ$ backward secondary step was applied during both rightward and leftward $10^\circ$ primary saccades, which simulated a sudden 20% bidirectional increase in saccadic gain by causing the animal to consistently overshoot the target. As shown in Fig. 2B (animal #1, rightward saccades), the animal reacted to the repeated overshoots by decreasing the intrasaccadic version position change. The grey dots are the 50 initial $10^\circ$ rightward controls. Trial #1 is defined as the first trial of the actual experiment. The red traces are single adaptive constant exponential fits. With the progress of the adaptation related to the number of exposures to each specific landing error and not to the actual session time, we adopted for the exponential fits the term “adaptive constant” as being more appropriate than the more usual term “time constant”. The value labeled $\Delta_{AS}$ is the asymptotic amplitude of the exponential in degrees, and $A_C$ is the adaptive constant expressed as a function of the total number of trials. In the fully-predictive design, the actual number of exposures to each landing error (rightward vs. leftward $10^\circ$ primary steps) is $\frac{1}{2}$ of the total number of trials. As a general feature observed in both human and monkeys, our two animals found decreasing the gain to be easier than increasing it, as can be seen in Fig. 2 by comparing the adaptive constants $A_C$ for the increasing (Panel A) and decreasing (Panel B) sets. Panels C and D illustrate our search, in the same data reported in Panels A and B, for any evidence that bi-ocular adaptation is a binocular process, in the sense that it alters the gain of a common version drive to the two eyes, or a monocular process, where
the gains of the two eyes are independently adjusted. In the first case, we expected little or no alteration in conjugacy, i.e., the level of correlation of the intrasaccadic changes in eye position in the two eyes, between corresponding control and adaptive sets. In the second case, some significant differences were expected, considering it unlikely that the independent right-eye and left-eye adaptive elements would generate exactly identical gain changes and with exactly identical adaptive constants.

We therefore computed the linear regression between the intrasaccadic horizontal position change of the left eye and of the right eye for all the experimental data in each bi-ocular control and adaptive session (Trial # >=1). In the 8 bi-ocular fully-predictive design adaptive sets (2 animals, + and −20%, rightward and leftward saccades) the R² ranged from 0.88 to 0.97 (mean 0.91±0.03 SD), while for the associated controls it ranged from 0.87 to 0.98 (mean 0.94±0.04 SD). For the control sets we computed the R² after we restricted the intrasaccadic version range inside each set to match the version range of the correspondent adaptive set, in order to avoid overestimating the control R² by computing it on the wider intrasaccadic range of responses present in the control sets. A mean paired t-test between the 8 correspondent adaptive and control sets was not significant (P=0.08). Furthermore, adding trial # as an independent variable in the linear regression improved the R² of the adaptive sets by at most 2%, and its contribution was often not significant. Finally, we plotted the changes in intrasaccadic vergence as a function of trial #, and no discernible pattern was observed in animal #1. In animal #2, there was a small significant increasing convergence for rightward saccades and a small significant increasing divergence for leftward saccades in all sets, adaptive and control, as the session progressed. Thus, it had no relationship with adaptation or its sign. We could not determine if this was an unspecific slight change in gain in one eye with time, or a change in the accommodation/vergence dissociation that was also dependent on saccadic direction. Overall, we found no evidence, in the fully-predictive bi-ocular sets, of adaptation altering conjugacy.
The temporal progress of the version adaptation in the bi-ocular fully-predictive design was similar, inside each session, for the two saccadic directions. This is illustrated in Fig. 3 (FIGURE 3 NEAR HERE), which reports the exponential fits of the four rightward/leftward pairs (session with bidirectional simulated gain increases, session with bidirectional simulated gain decreases, two animals), expressed as intrasaccadic version gain (1 equivalent to 10°) of the primary saccade. For the gain increases in animal #2 the exponential fit did not converge (sets identified with an asterisk) and we used a linear fit, defined by the slope $S_L$. ASE, in parenthesis, is the asymptotic standard error. The value TN in Fig. 3 is the experiment trial number when the animal stopped working, and the actual range of trials on which the fits were computed. For clarity, the plots are limited to the first 1500 trials. The value $\Delta$ indicates the total version gain change, in %, achieved during the session, defined as the % difference between the value of the fit at trial number TN and at trial number 1. For these sets, version full adaptation is +20% or -20%. The symbol # near the $\Delta$ value indicates that the animal achieved adaptive steady state for that set during the session, which was defined as a set where TN was more than three times $A_C$. The value $\Delta$ in these sets is practically the asymptotic amplitude of the exponential expressed as % of gain change. Both animals achieved the steady state for the gain decreases, and animal #1 for one gain increase (rw +20%). Animal #1 achieved good adaptation in all four cases. Animal #2 had clear difficulties with the gain increases, while having a robust adaptation for the gain decreases, albeit with smaller asymptotic values compared to animal #1.

DYNAMICAL ANALYSIS OF ADAPTED SACCADES. As a first analysis of the dynamics of the adapted saccades in the bi-ocular fully-predictive paradigm, we compared the average version velocity profile of the last fifty 10° rightward and of the last fifty 10° leftward saccades in the bi-ocular adaptive sessions (BA in Fig. 1) with, respectively, the average version velocity profile of the last fifty rightward and the last fifty leftward 8°, 10°, and 12° saccades from the associated control sessions (BC in Fig. 1) to take into account the changes in saccadic dynamics due to fatigue (Straube
This approach was preferred to a comparison made on adaptive and control trials within the same range of trial # because it probably better matched the animal alertness and interest in the primary saccadic task. The two upper panels in Fig. 4 (FIGURE 4 NEAR HERE) show an example of a backward-step adaptive case (animal #1, bi-ocular -20% adaptive paradigm, fully-predictive design, rightward saccades). Panel BA illustrates the average version position (HVS) and version velocity (HVS) of the last 50 rightward saccades (continuous lines) of the adaptive set, with the dotted lines the ±SD. All traces were synchronized with respect to primary saccade onset before averaging. The decrease in gain near the end of this session was quite robust, as evident in panel BB, which compares the adapted position and velocity version averages from Panel BA (traces labeled -20% AD) with the averages of the last fifty 8° (CONT) and 10° (CONT) saccades of the correspondent control session. The adapted saccades had profiles, on average, similar to gain-reduced 10° “fatigued” control saccades. This opens the possibility of the adapted saccades being elicited by the primary steps as 10° saccades unaltered by the adaptive process, only further downstream scaled down by the adaptation. Note, as evident in panel BB, that this mechanism would make the adapted saccades appear slower and last longer than similarly “fatigued” 8° control saccades if, for that animal, following the duration/size main sequence (Bahill et al. 1975), 10° control saccades are of significantly longer duration than 8° control saccades. No actual adaptive dynamical changes would have occurred, just an amplitude decrease of larger and longer 10° saccades. The two lower panels FA and FB show an example of a forward-step adaptive case (animal #1, bi-ocular +20% adaptive paradigm, fully-predictive design, rightward saccades) with the same layout. In Fig. FB, the adapted averages (+20% AD) from panel FA are now compared with the averages of the last fifty 10° (CONT) and 12° (CONT) saccades of the control session. The profile was, again, similar to gain-altered 10° “fatigued” control saccades. In this case, if the animal had its 12° control saccades significantly longer in duration than its 10° control saccades (not true for this set), adapted saccades obtained by upward
rescaling of 10° saccades would actually appear faster than 12° control saccades at a similar level of fatigue. We attempted to quantify these dynamical changes for both control and adaptive sets by morphing the average version velocity profile of the initial fifty 10° same-direction control trials of the session onto the version velocity profile of each associated experimental trial (TN≥1). This morphing was obtained with a minimum square error procedure that quadratically altered the time scale and linearly the amplitude scale of the associated control average profile. This was seen as a much more robust estimate of the temporal alteration of the main component of the saccade than standard point-wise duration and amplitude measures. The vast majority of both control and adaptive sets (bi-ocular, uni-ocular, and symmetric) showed highly significant increases in duration of the version velocity profiles with trial # with respect to the initial fifty 10° controls of the session, quantified as a significant deviation of the distorted time scale from the 1:1 line (no time distortion). Most interestingly, there were no consistent differences in the level of time distortion between bi-ocular (BC vs. BA), uni-ocular (UC vs. UA) or symmetric (SC vs. SA) control and adaptive sets. This was also true for the pseudo-random paradigms, strongly suggesting that an unspecific fatigue effect, shared with the controls, was most likely the cause of the increase in duration of the version velocity profiles of the adapting saccades as the session progressed. For the uni-ocular and symmetric cases, part of the saccadic slowing might have been caused by vergence-saccadic interactions, which are known to generate slower and longer saccades (Collewijn et al. 1995; Walton and Mays 2003), but we did not see an additional slowing in these sets when compared with the bi-ocular sets. In both fully-predictive and pseudo-random bi-ocular paradigms, we also attempted to see if the adapted profiles, as amount of time distortion, were significantly different from the last fifty 8° saccades in the control sets in the -20% cases and from the last fifty 12° saccades in the control sets in the +20% cases (Fig. 4), supporting the concept that adaptation in the bi-ocular paradigms is a downward or an upward linear gain scaling of unadapted 10° primary saccades. The alternative hypothesis was for the adapted
saccades to be generated directly as 8º or 12º movements, respectively, and therefore having dynamics
similar to control 8º or 12º saccades. The results were inconclusive. Perhaps slight differences in the
fatigue level between the control and adaptive sessions, acquired on different days, were sufficient to
mask the small dynamical differences that would have allowed us to determine the mechanism of bi-
ocular adaptation, although it is also possible that bi-ocular adapted saccades do not follow the
unadapted main sequence.

EXTRASACCADIC ADAPTIVE COMPONENTS. Are there contributions to the adaptation in the
bi-ocular paradigms outside the primary saccade, like presaccadic or postsaccadic smooth responses
or secondary saccades with short, non-visual latencies? As we will see later, smooth postsaccadic
components play an important role in uni-ocular and symmetric adaptation and, in the monocular
adaptive hypothesis, they also have to be present in the bi-ocular sets as, similar in the two eyes to
preserve conjugacy, adaptive monocular postsaccadic drifts. The scatter in Fig. 2 also raised the
question about the animals being truly engaged in the saccadic task. This was particularly important in
the fully-predictive paradigms where, due to their predictability, it was possible that the animals were
just following a rightward/leftward pattern to receive their reward without precisely following the
targets. Panel A in Fig. 5 (FIGURE 5 NEAR HERE) illustrates an example of the changes in
presaccadic version position from the onset of the primary 10º target step to the onset of the animal’s
primary saccade as a function of Trial # (animal #2, bi-ocular -20% adaptive paradigm, fully-
predictive design, rightward saccades). The animal had no anticipatory responses in the PR segment.
In the bi-ocular cases there were no presaccadic adaptive components, even in the fully-predictive
design. As described earlier, there was a rapid intrasaccadic adaptive change in version, evident when
comparing the 50 initial 10º controls (open grey circles) with the adaptive responses (open black
circles and filled grey circles) in Panel B. The amount of bi-ocular landing error introduced by the
secondary steps that was not compensated by the intrasaccadic version adaptation was accurately
corrected (Panel C) during the extended postsaccadic period (0-600 ms from primary saccadic offset). As the bi-ocular secondary steps were introduced, the total change in version position (from onset of the primary target steps to 600 ms after the end of the primary saccade) presented an immediate sharp transition from 10° to 8° (Panel D), indicating that the animal was fully engaged in the saccadic task to the very end of the session and carefully corrected the landing errors. The nature of the postsaccadic correction in Panel C is illustrated in Panel E, reporting the version position profiles and version velocity profiles, synchronized with respect to primary saccade offset, of the last 15 saccades of the session, identified with the filled grey circles in Panels A, B, C, and D. All post-saccadic corrections were visually-driven corrective saccades, as evident from their latency, longer than 180 ms from primary saccadic offset (the vertical dotted line identifies the location of the onset of the earliest corrective saccade in the set). To verify that these corrective saccades were truly linked to the residual postsaccadic visual error, for these 15 saccades we plotted the intrasaccadic version change of the primary saccade vs. the intrasaccadic version change of the corrective saccade (Panel F). The correlation was quite impressive ($R^2=0.76$). Neither bi-ocular sets in the fully-predictive nor in the pseudo-random design presented evidence of non-visual adaptive saccadic or smooth corrections preceding or following the primary saccade.

POSTSACCADIC DRIFTS. Although Fig. 5 suggests that (smooth) postsaccadic drifts, if present, do not play a significant role in bi-ocular adaptation, how adaptive saccades end is an aspect of particular importance for the understanding of the bi-ocular adaptive process. Is there evidence for an alteration in the immediate postsaccadic behavior between saccades subject to an increase in gain versus saccades subject to a decrease in gain, perhaps due to alteration in the pulse-step ratio (Robinson 1975)? The examples in Fig. 6 (animal #1, fully-predictive design, -20% or +20% bi-ocular adaptive paradigms, leftward saccades) (FIGURE 6 NEAR HERE) clearly show that this is not the case. All the traces used in Fig. 6 are synchronized with the offset of the primary saccade prior to averaging.
The two upper panels report the version velocity average (HVS±SD) of the fifty initial 10° leftward control saccades (left panel) and of the last fifty leftward adapted saccades (-20%) of this bi-ocular adaptive session (right panel). The magnified plots of the trace segments identified by the blue boxes in the main figures show the averages of the horizontal version velocity HVS, horizontal left eye velocity HL, horizontal right eye velocity HR, and vergence velocity VG. The postsaccadic overshoots were very similar between the 50 initial controls of the session and the last 50 adapted saccades. Strikingly, practically identical overshoots were present in the +20% case, illustrated in the two lower panels using the same layout.

To better elucidate the development in time of the bi-ocular postsaccadic drifts as the adaptive sessions progressed, Fig. 7 (FIGURE 7 NEAR HERE) shows examples of the time course of the changes in horizontal right eye position (panels A and E), horizontal left eye position (panels B and F), vergence position (panels C and G), and horizontal version position (panels D and H) in the first 50 ms time interval after the end of the primary saccade (PO[0-50] measures) as a function of trial #. The upper panels report the data for the rightward saccades in the -20% bi-ocular adaptive fully-predictive session in animal #2. The lower panels report the same measures for the leftward saccades in the same session. The quality of the measures is quite remarkable, with clear and highly significant changes occurring inside the PO[0-50] interval as the session progresses, particularly for the horizontal version measures. The red lines are second-order polynomial fits. The asymmetries between the right-eye measures and the left-eye measures are most likely due to the divergence/convergence transients, in this late part of the response being convergence responses (positive sign of the vergence measures in panels C and G). The inversions with saccadic direction in sign and trend with trial # of the version measures are quite evident when comparing panels D and H. For both rightward and leftward saccades, the movement ends with small overshoots (negative values for rightward saccades, positive values for leftward saccades) presenting a clear trend to decrease their amplitude as the session
progressed. To verify if these results are specific to the bi-ocular adaptive paradigms or if they also apply to the control sets, Fig. 8 (FIGURE 8 NEAR HERE) shows the second order polynomial fits of the PO$_{[0-50]}$ horizontal version measures for the two bi-ocular fully-predictive adaptive sets and for the associated control sets superimposed (animal #1 in the left panel, animal #2 in the right panel). The postsaccadic horizontal version overshoots are clearly determined by saccadic direction (rw or lw), with direction of the adaptation (+20% or -20%) having a small, if any, impact on their time course when compared with the controls (CONT). Identical results were found in the bi-ocular sets following the pseudo-random design. It is likely that the decrease in the amplitude of the overshoots is another unspecific aspect of fatigue, with the PO$_{[0-50]}$ values gradually converging toward zero for both control and adaptive sets. The data show no evidence of the postsaccadic drifts being affected by or contributing to bi-ocular adaptation, or, indirectly, of adaptation affecting the pulse-step ratio of the primary saccade. Bi-ocular adaptation seems to equally scale the pulse and the step components of the primary saccade.

SUMMARY. Our analysis of the bi-ocular adaptive results in the fully-predictive design suggests that the adaptive process in these paradigms is likely conjugate and strictly limited to the main component of the primary saccade. There were no presaccadic adaptive contributions, and the analysis of the PO$_{[0-50]}$ postsaccadic drifts identified them as overshoots related to the saccadic direction and not to the adaptive process. The oculomotor responses inside the PO$_{[0-600]}$ interval were found to be visually-driven corrective saccades. These observations also extended to the bi-ocular data in the pseudo-random design, which are not shown for brevity. We also found that the changes in version dynamics observed in the adapted saccades were mostly non-specific effects due to fatigue, and this observation, not shown for brevity, also extended to the uni-ocular and symmetric paradigms and to both fully-predictive and pseudo-random designs.

*Fully-predictive design uni-ocular and symmetric paradigms*
GENERAL OBSERVATIONS. If saccadic short-term adaptation is a monocular process, where each eye recalibrates its gain independently from the other on the basis of its own landing errors, the adaptive behavior for the uni-ocular and symmetric paradigms will necessarily match the adaptive behavior described above for the bi-ocular paradigms. A bi-ocular adaptation, in this view, is simply a monocular adaptation where both eyes receive the same secondary steps, and therefore the right-eye and left-eye monocular gain controllers are asked to achieve identical gain changes. In the uni-ocular paradigms, the eye seeing the backward or forward 20% secondary step will adapt exactly the same way it does in the bi-ocular paradigms, unaware that there is no secondary step in the other eye. In the symmetric paradigms, each eye will adjust its gain by equal and opposite half amounts. Furthermore, postsaccadic drifts in the PO [0-50] interval are expected to give no contribution to the adaptive process and only to depend on saccadic direction and fatigue. Already at the single trial level things look quite incompatible with the monocular view, with three single-trial examples reported in Fig. 9 (FIGURE 9 NEAR HERE) (animal #1, +20% uni-ocular step on the right eye, leftward saccades). The upper panels report eye positions (left eye LE, right eye RE, vergence VG) together with the calibrated feedback signals from the mirrors (left eye mirror LT, right eye mirror RT). The middle panels report eye velocities with the same color scheme. Traces are synchronized with the onset of the primary target steps. The initial fifty 10⁹ primary-only trials were obviously not different from the initial fifty primary-only trials in the bi-ocular sets. Panel A reports one of them to highlight the vergence transient, also present in these initial control saccades. In the initial adaptive trials, where there was no time for adaptation to have developed, the primary saccades were also identical to the initial primary-only controls as expected. One example is reported in Panel B. The first striking difference with respect to the bi-ocular case (compare with Fig. 5 panel E) is that the visual correction of the disparity error introduced by the secondary step being applied to only one eye is achieved by a smooth vergence response. Small corrective saccades could also be present in the VISUAL time interval to
compensate for the 10% change in version introduced by the unbalanced secondary step (Fig. 1 UA case). The second is that even in the cases where the animal achieved adaptive steady state, a large postsaccadic component was present after the end of the primary saccade (arrow). As the asterisk near the vergence velocity trace in panel C indicates, some presaccadic vergence responses were also present in some trials.

With the data reported in Fig. 9 from a fully-predictive set, we initially suspected that what we were observing was a vergence-driven predictive process, where the smooth visually-driven vergence correction of the disparity error introduced by the uni-ocular secondary step (Panel B) gradually travelled in the direction of the saccade (Panel C) driven by prediction. To test this hypothesis, we plotted the changes in vergence position ($\Delta VG$) in the IN, PO$_{[0-50]}$, VIS$_{[0-100]}$, and VIS$_{[100-200]}$ intervals as a function of Trial # (lower panels in Fig. 9). These time intervals are identified in the single-trial panels as vertical dashed lines, and are labeled in Panel C. Following this hypothesis, as the vergence wave travelled toward the saccade we expected a gradual decrease in the VIS$_{[100-200]}$ values and at least a transient increase in the VIS$_{[0-100]}$ values. During the time needed for this wave to encroach the saccade, the IN and PO$_{[0-50]}$ values were expected to remain stationary at least for a short period. In all adaptive uni-ocular and symmetric fully-predictive paradigms, the values in VIS$_{[0-100]}$ remained pretty flat throughout the session or showed a trend toward zero, and no initial plateaux in the IN or PO$_{[0-50]}$ measures were detected. Furthermore, the same behavior was observed in the uni-ocular pseudo-random paradigms, where prediction was not expected to play a role. The behavior described in these panels is much more consistent with the development of a perisaccadic adaptive process influencing both the IN and the PO$_{[0-50]}$ measures, and with the postsaccadic visually-driven vergence corrections, stationary in latency, becoming smaller and smaller as the perisaccadic adaptation increased.

POSTSACCADIC COMPONENTS. For a given saccadic direction, identical disparity landing errors can be generated by a decrease in gain in one eye or by an identical increase in gain in the other eye.
For example, for rightward saccades we can introduce a crossed disparity error by applying a backward secondary step in the right eye or by applying a forward secondary step in the left eye. Both paradigms require a convergence adaptive response. In a binocular adaptive modality, this convergence response will be driven by the vergence system and will symmetrically affect both eyes, with the direction of the primary saccade and which eye saw the step being irrelevant factors. In a monocular adaptive modality, we will have an adaptive response affecting only the eye that saw the secondary step, with the uni-ocular adaptation achieved by pure asymmetric saccades (Fig. 5E). From the bi-ocular results, we also expect, in the monocular modality, any postsaccadic drift to be only related to saccadic direction. The upper section of Fig. 10 (FIGURE 10 NEAR HERE) illustrates the averages of the velocity profiles, after alignment with saccadic offset, of the initial fifty rightward 10° primary-only saccades (left panels) and of the last fifty rightward adapted saccades (right panels) in the two uni-ocular fully-predictive rightward saccades convergence sets (-20% secondary step on the right eye and +20% secondary step on the left eye) from animal #1. The layout is similar to Fig. 6, with the only difference that the dashed ±SD of the HVS traces in the main panels in Fig. 6 are now the HL (red) and HR (green) velocity averages. Horizontal version velocity averages (HVS) are in black and vergence velocity averages (VG) are in violet. The similarities in adapted average postsaccadic profiles between the -20% secondary step on right eye and the +20% secondary step on the left eye are truly striking, clearly suggesting the presence of a symmetric adaptive convergence response affecting both eyes. Note that these data are from different days. The lower part of Fig. 10 illustrates the averages, with identical schema, of the velocity profiles in the two uni-ocular fully-predictive rightward saccades divergence sets (+20% secondary step on the right eye and -20% secondary step on the left eye) from animal #1, also acquired on different days. Again, the evidence is for the presence of a symmetric adaptive divergence response affecting both eyes. Similar results were obtained in the fully-predictive symmetric and the pseudo-random uni-ocular paradigms.
VERSION ADAPTATION. If the hypothesis suggested by Fig. 10 about the presence of a saccadic-controlled symmetric adaptive vergence response is correct, it is possible that the version landing errors and the disparity landing errors are dealt with by independent adaptive mechanisms. This would mean that the adaptation to the 1° version landing errors introduced by the uni-ocular 2° secondary step is a version-only process that necessarily follows the same behavior observed in the bi-ocular adaptive paradigms. In the context of the immediate postsaccadic behavior, this implies the version responses in the PO_{[0:50]} interval are non-adaptive saccadic overshoots, i.e., determined only by the saccadic direction, that gradually converge toward zero as the session progresses due to fatigue. This hypothesis also requires that they are unaffected by which eye experienced the secondary step and by its sign. Furthermore, the intrasaccadic version adaptation (IN time interval) will have adaptive constants similar to the bi-ocular data, and to present the typical asymmetry between increasing and decreasing gain paradigms. The data presented in Fig. 11, (FIGURE 11 NEAR HERE) from animal #2, clearly support a version-only adaptation that is acting independently of the mechanism dealing with the correction of the disparity landing errors. Panel A illustrates the single-trial changes in horizontal version position in the PO_{[0:50]} interval for the leftward saccades in the +20% uni-ocular step on the right eye paradigm as a function of Trial #. Panel C shows the same measure for rightward saccades in the -20% uni-ocular step on the right eye paradigm. Both are convergence tasks, but the PO_{[0:50]} version measures clearly have opposite sign and follow similar trends toward zero. The red lines are second order polynomial fits, which are used in Panels B and D. With a striking similarity with this animal’s bi-ocular behavior, reported in Fig. 8 right panel, Panel B shows that the immediate post-saccadic version drifts for leftward saccades for all uni-ocular fully-predictive paradigms, irrespective of the sign of the disparity or which eye saw the step, were overshoots (positive sign) with a trend toward zero as the session progressed. Mirror-image results were observed for rightward saccades (Panel D). The associated uni-ocular controls (not shown) gave
very similar results, again supporting the observation, made with the bi-ocular sets, that version adaptation does not affect the immediate post-saccadic behavior. This pattern was confirmed in the uni-ocular fully-predictive paradigms in animal #1 and in the fully-predictive symmetric paradigms in both animals. In the pseudo-random uni-ocular sets, due to the saccades ending at different version position values (Fig. 1), there was more scatter in the postsaccadic version overshoots, but the behavior, again, was not affected by the direction of the disparity error or by which eye saw the step. Overall, the version behavior in the PO\(_{[0,50]}\) interval was practically identical to the bi-ocular data. As for the bi-ocular paradigms, the presaccadic version behavior showed no evidence of presaccadic version contributions to the adaptive process. Thus, version adaptation was found to be strictly limited to the intrasaccadic period as in the bi-ocular cases. The lower section of Fig. 11, with a similar layout, illustrates the version position changes in the IN period for the same sets in the upper section. The only difference is that panels F and H now report the intrasaccadic version gain of the primary saccade, and the fits are single adaptive constant exponential or linear fits. The similarities with Fig. 3 Animal #2, reporting the same measures for the bi-ocular sets of this animal, are evident, even if the version adaptation goal is only half of the bi-ocular case. The very strong bi-ocular asymmetry between increasing version gain and decreasing version gain in this animal is preserved in the uni-ocular sets. The adaptive constants are very similar to the bi-ocular sets, and independent of which eye saw the step and/or the direction of the disparity error. Identical results were obtained from animal #1. No version errors are introduced in the symmetric paradigms, and, accordingly, the data showed no consistent version changes as the sessions progressed. In summary, the version analysis for the bi-ocular and uni-ocular paradigms strongly suggests that version saccadic adaptation is an independent, likely conjugate, adaptive process strictly limited to the intrasaccadic period. We also have preliminary evidence (Figs. 9 and 10) that adaptation to the disparity landing errors might be
achieved by saccadic-controlled symmetric vergence responses in the two eyes, which behavior we will explore next.

VERGENCE DYNAMICS. Similar to the version dynamical analysis for the bi-ocular data illustrated in Fig. 4, for the uni-ocular and symmetric paradigms we compared the vergence position and velocity profiles of the last 50 trials of the adaptive sessions with the last 50 trials of the associated control sessions. Traces were synchronized with respect to the onset of the primary saccade. As evident in the single trial in Fig. 9 Panel A, the initial fifty 10º control saccades of both control and adaptive sessions already presented a pronounced vergence response, usually termed the “vergence transient”, which is also present in saccades with no net change in depth (Busettini and Mays 2005a; Sylvestre et al. 2002; Maxwell and King 1992; Collewijn et al. 1988). Figure 12 (FIGURE 12 NEAR HERE) presents data from the +20% uni-ocular step on the left eye control and adaptive paradigms in the fully-predictive design from animal #1. Rightward saccades (upper panels) are associated with a crossed disparity, and leftward saccades (lower panels) with an uncrossed disparity. The vergence transients in the fifty primary-step only 10º initial controls (first and third columns) were almost machine-like, although with some variability between the daily sessions. This reproducibility is consistent with the vergence transient being the result of a dynamical asymmetry of the abducting and adducting elements of the oculomotor plant (Zee et al. 1992) and not an active vergence response (but see Sylvestre et al. 2002), although temporal differences in the premotor drives between the two eyes are also possible (Zee et al. 1992; Maxwell and King 1992). Some of this daily variability is likely due to small variations in the right-eye and left-eye calibrations. With the peak version velocity of 10º saccades as high as 400 º/s, even a small 1% gain calibration error in one eye would introduce a 4 º/s distortion in the intrasaccadic vergence velocity profiles. Small variations in the offset adjustments and thermal drifts of the mirror galvanometers or of the coil detectors may also play a role, although we turned the laboratory on at least one hour before the start of the session to thermally stabilize the
electronics and recalibrated coil detectors and galvanometers daily. The trial-by-trial reproducibility of the last fifty rightward and leftward trials in the session is also remarkable, if one considers that these are the last saccades of the session before the animal stopped working. The key observation is the striking similarity in vergence dynamics between the last fifty saccades in the control and the adaptive sessions, particularly remarkable for the rightward saccades set of this example. The strong similarity is also present for the leftward saccades if one visually subtracts from the last fifty vergence profiles the profile differences in the control vergence transients between the control and the adaptive sets. This is quite surprising, if one considers that in the control paradigms the vergence responses are driven by a visual disparity, while in the adaptive paradigms they are the non-visual result of a saccadic adaptation. The slowing of the late saccades when compared with the initial controls is also quite evident in both control and adaptive paradigms by observing the change in average version velocity profiles (grey dotted lines in the average plots).

DEVELOPMENT IN TIME OF THE VERGENCE ADAPTATION. The analysis of the vergence adaptive process was similar to the analysis of the version components. The presaccadic analysis showed some smooth vergence preceding the primary saccades in both control and adaptive sets, particularly for late primary saccades, like the example in Panel C in Fig. 9. The overall contribution was small, and mostly indicated that smooth vergence adaptive contributions can precede the primary saccade, as visually-driven smooth vergence contributions often precede the primary saccade in 3-D gaze transfers. Our main focus was on three measures: IN, PO[0-50], and PREVISUAL changes in vergence position. The PREVISUAL (PR + IN + PO[0-50]) measure derives from the observation that smooth vergence responses can precede the primary saccade, i.e., anticipate the onset of the pause of the OPNs associated with the primary saccade, and can continue after the OPNs have resumed their baseline firing (van Horn et al 2008; Busettini and Mays 2003). Therefore, PR and PO[0-50] contributions are an integrant part of the non-visual vergence adaptive process, making PREVISUAL
a more appropriate measure of the vergence adaptation than the intrasaccadic (IN) measure. Adaptive non-visual components may also be present during the initial VISUAL period, and add to the responses elicited by visual feedback but, being indistinguishable from visually-driven responses, we could not include them in the computation. The PO\([0-50]\) vergence analysis will test if the postsaccadic component in Fig. 9 Panel C (arrow) is a true vergence adaptive component.

Sample single-trial measures are reported in Fig. 13 (FIGURE 13 NEAR HERE) from two convergence and two divergence uni-ocular fully-predictive sets from animal #2, with the secondary steps applied to one or the other eye. The first column reports the change in vergence position inside the intrasaccadic (IN) interval, the second column inside the PO\([0-50]\) interval, and the third column inside the entire PREVISUAL interval, all as a function of trial #. The fourth column illustrates an estimate of the relative contribution of the intrasaccadic (IN) change in vergence with respect to the entire PREVISUAL change. In the first three columns, the red lines are single adaptive constant exponentials, while the red lines in the fourth column are second order polynomial fits. Note that the y-scale factor for the PO\([0-50]\) data is twice as large with respect to the IN and PREVISUAL plots for clarity. Also, plots of sets with more than 1500 adaptive trials were truncated at 1500, although the fits were computed using the entire set. The key difference with respect to the version adaptation is that the PO\([0-50]\) vergence position change is a robust adaptive component, necessarily driven by the vergence system. The saccadic system is inhibited by the OPNs from the start of the postsaccadic period. It is also evident, from the plots in the fourth column, that there is a precise ratio between the IN and the PREVISUAL vergence contributions. The dashed line represents the entirety of the PREVISUAL response being contained inside the intrasaccadic period. As the overall PREVISUAL adaptive contribution increases, the IN relative contribution decreases, with more adaptive contribution coming from the PO\([0-50]\) interval and also from the small presaccadic vergence responses, if present. An important feature of the plots in the fourth column is the absence of any
evident breaking point that would suggest that up to a certain PREVISUAL value the saccadic system can monocularly deal, strictly intrasaccadically, with the disparity correction by itself, and only after a certain threshold must rely on the vergence system, solely responsible for the postsaccadic component. The properties illustrated in Fig. 13 are accurately preserved irrespective of the eye seeing the uni-ocular secondary step or the crossed or uncrossed disparity landing error, and, for the PO\([0-50]\) measures, irrespective of the saccadic direction. With the evidence that the PO\([0-50]\) vergence responses are integrant contributions to the vergence adaptive process, the analysis of the adaptive constants in the next section was performed on the PREVISUAL vergence measures.

VERGENCE ADAPTIVE CONSTANTS. Critical evidence in support of an independent saccadic-controlled, but vergence-driven, adaptive mechanism dedicated to the correction of post-saccadic disparity landing errors would be that the time course of the adaptation is determined by the sign of the disparity error alone, with saccadic direction, which eye saw the step, or the modality of how the error was introduced (uni-ocular or symmetric) being mostly irrelevant factors. The two top panels (animal #1 and animal #2) in Figure 14 (FIGURE 14 NEAR HERE) report the single adaptive constant exponential or linear fit of the adaptive change in vergence position inside the PREVISUAL interval as a function of trial # for all the uni-ocular fully-predictive design sets. The first table, with layout and symbols identical to the tables in Fig. 3, with the exception of the version gain being replaced by the vergence change in degrees, applies to the same sets illustrated in the two top panels. One property is immediately apparent. The time course of the vergence-driven adaptation is univocally determined by the sign of the disparity introduced by the secondary step, independently of saccadic direction, which eye saw the step, and most importantly, the sign of the secondary step. Increasing or decreasing the gain of one eye, which directly affects, also in these data, the time course and amount of the version adaptation, is an irrelevant factor for the vergence-driven adaptation. Most humans and monkeys, including our two animals, presented visually-driven convergence responses
that were somewhat faster than similar-size divergence responses (Hung et al. 1997). This is also
reflected in the rate of adaptation ($A_C$ or $S_L$) and the PREVISUAL amount of adaptation in degrees
achieved during the session ($\Delta$) between convergence and divergence sets, the latter estimated as the
difference of the value of the fits at trial TN and at trial #1. The vergence velocity trace $\hat{V}_G$ in Panel C
in Fig. 9 suggests that the adaptive response can extend into the VIS$_{[0-100]}$ interval (arrow). Our $\Delta$
values, which ignore these responses, are probably underestimations of the overall vergence-driven
adaptation, but we preferred to strictly limit our measures to the previsual period. Vergence adaptation
steady state was reached in only one set (symbol # in the $\Delta$ column), vergence adaptation being, on
average, slower than version adaptation.

The analysis of the symmetric fully-predictive design data (bottom table of Fig. 14) did not
unmask any indication for these adaptive paradigms to be harder than uni-ocular paradigms.
Divergence adaptation was, again, harder to achieve than convergence adaptation. In a uni-ocular
paradigm, the requirement is to increase or decrease the gain in one eye while leaving the gain in the
other eye as unchanged as possible. In the symmetric case, there is the need for a gain increase in one
eye and a gain decrease in the other eye for the same saccadic direction, which conflicts even more
with the default gain co-variation in the two eyes observed when adapting one eye while the other eye
is patched (Albano and Marrero 1995; Snow et al. 1985; Optican and Robinson 1980; Abel et al.
1978). For an independent saccadic-controlled but vergence-driven correction of the disparity landing
errors, the two paradigms are functionally identical, the presence or absence of a simultaneous version
landing error being irrelevant.

RELATIVE WEIGHT OF POSTSACCADIC VERGENCE CONTRIBUTIONS. The panels in the
fourth column of Fig. 13 suggest that, for the adaptive data, there is a precise relationship between
total vergence change in the PREVISUAL period and the intrasaccadic (IN) period. If the vergence
responses in the 3-D gaze transfers and in the adaptive paradigms share the same downstream circuits
and also the same vergence-saccadic interactions, we expected the postsaccadic vergence “leaks”, i.e.,
the deviations from the 1:1 lines to also be similar. This is tested in Fig. 15. (FIGURE 15 NEAR HERE),
which reports the second order polynomial fits of the vergence position change in the
IN(trasaccadic) interval as a function of the vergence position change in the PREVISUAL interval
(similar to Fig. 13 fourth column) for all uni-ocular fully predictive adaptive (in color) and associated
controls (grey) sets. The control fits (in grey) also include the initial fifty rightward and leftward
primary-only saccades to overlap in range with the adapted data at the beginning of the adaptive
process. There is a clear continuity in the deviation from the 1:1 line between the adaptive and control
sets for both divergence and convergence tasks. The larger the amount of previsual vergence, the
smaller is the relative contribution of the intrasaccadic vergence and, consequently the larger the
presaccadic (if present, and usually very small for <3º vergence changes associated with 10º saccades)
and postsaccadic vergence contributions. There was no evidence, for both control and adaptive sets,
of a breaking point that would suggest that only after a certain threshold in the asymmetry the
saccadic system has to rely on the vergence system, which is solely responsible for the postsaccadic
“leaks”.

Pseudo-random design paradigms

The technical issues related to the setting up and the analysis of the pseudo-random
experiments were truly daunting, from the non-linear tables that we had to implement to drive the
mirror galvanometers for the targets to follow the trajectories in space illustrated in Fig. 1 to the
difficulties in precisely calibrating the eyes inside much larger version and vergence ranges.
Furthermore, half of the data (the 5º primary saccades) could not be used, and the vergence transients
were found to depend on the eye eccentricity at the start of the saccade. Nonetheless, we needed to
address the issue of if our fully-predictive results, much easier to obtain and also easier on the animal
from a behavioral point of view, were some kind of predictive artifacts, and therefore not
representative of the saccadic adaptive mechanism. The pseudo-random design is much closer to what a subject with altered saccadic gains experiences in the real world. This is even more important to know before implementing single unit experiments, which are extremely time consuming and have very low outputs.

BI-OCULAR PARADIGMS. The bi-ocular pseudo-random design had four adaptive experiments and associated controls, with same or opposite gain changes for the two saccadic directions, the latter not feasible in the fully-predictive design. In the upper panels in Fig. 16 (FIGURE 16 NEAR HERE), which follows the same layout of Fig. 3, we used a color code to identify each of the four bi-ocular adaptive sessions. The fact that in the pseudo-random design each adaptive trial type was presented only ¼ of the time and that the animal could not predict the size of the saccade (5° or 10°) or, sufficiently away from the edges of the stimulus ranges, its direction, had little effect on the time course of the adaptation or its amount ($\Delta$), particularly for the decreases in gain (-20% traces). Asking for an increase in gain in one saccadic direction and a decrease in the other (green and black traces) also had minor effects. In the pseudo-random design, gain increasing was even harder than gain decreasing, now quite evident also in animal #1, and half of the gain increasing sets, identified with an asterisk, had to be fitted with a linear regression. Interestingly, even when the animal reached the adaptive steady state (sets with # in the $\Delta$ entry), the $\Delta$ for gain increases was consistently smaller than the $\Delta$ for gain decreases, indicating it was not just a different speed of the adaptive process. It is also evident that the time course for the gain increases was more variable between sessions. The intrasaccadic version gain change for the lw +20% matched in the same session with the rw -20% (black code) in animal #2 and reported in grey in the table below the panels was not significant. On the contrary, the adaptive process was remarkably consistent for gain decreases. The overall average adaptive constant for gain decreases in the bi-ocular pseudo-random design sets (4 cases, 2 animals) was 252 (± 56 SD; range 173 to 370; n=8). This is remarkably similar to the average value for the
fully-predictive design (2 cases, 2 animals), which was 253 (± 87 SD; range 196 to 381; n=4). The Δ values were also practically identical: -15.5 (± 3.6 SD; range -20.5 to -9.8; n=8) for the pseudo-random design and -16.3 (± 2.3 SD; range -18.6 to -14.1; n=4) for the fully-predictive design. For the gain increases, the Δ was better in the fully-predictive design for animal #1, and this is probably also true for animal #2 if we consider that in the two fully-predictive sets the adaptation was still increasing linearly when the animal lost interest in the task.

We also repeated all the other bi-ocular version analyses described for the fully-predictive design. We confirmed, also for the pseudo-random design, that conjugacy is not altered by the adaptive process, the adaptation is strictly limited to the intrasaccadic period, and that the post-saccadic drifts are related to saccadic direction and do not contribute to the adaptation. Overall, the data do not support a different bi-ocular adaptive mechanism for the two designs, and with prediction playing only a minor, inconsistent role.

UNI-OCULAR PARADIGMS. Very similar results, although somewhat noisier, were obtained when comparing control and adaptive uni-ocular vergence profiles in the pseudo-random design, likely due to the variation in the vergence transients along the entire version and vergence ocular ranges covered by these paradigms. Version and vergence adaptive processes were again clearly dissociated in terms of adaptive constants and post-saccadic behavior. The uni-ocular pseudo-random design data (lower table in Fig. 16) presented PREVISUAL vergence adaptive constants and Δ values that were similar to the values obtained for the fully-predictive sets (compare with upper table in Fig. 14), indicating, as for the version adaptation in the bi-ocular and the uni-ocular tasks, that prediction has little, if any, impact on the adaptive process. Overall, the simpler fully-predictive design veridically represented the saccadic adaptive processes.
DISCUSSION

Why a binocular short-term saccadic adaptive process?

Primates have binocular vision. From a sensory point of view, a saccadic system that relies on a version-driven adaptive mechanism to recalibrate its cyclopean (conjugate) responses and on a vergence-driven adaptive mechanism that relies on postsaccadic disparity information to maintain binocular alignment makes perfect sense. On the contrary, from a point of view of recovery from pathology/injury along with the effects of aging, an independent monocular recalibration of the two eyes would be much better optimized to deal with focal damages or deficits at the level of single extraocular muscles or their innervation. Surprisingly, we found no behavioral evidence, using the double-step saccadic paradigm, of a monocular mechanism. Our results support a saccadic adaptive mechanism that relies on the visual detection of consistent postsaccadic disparity errors to generate, during the motor planning of the saccade, an internal compensatory disparity signal, which is then sent to the vergence system to reestablish binocular alignment. Consistent postsaccadic version errors generated independent, likely conjugate, recalibrations of the version commands. The ratio between the (IN)trasaccadic vergence response and the overall PREVISUAL response (Fig. 13 4th column, and Fig. 15) did not present, in both control and adaptive paradigms, breaking points suggesting a disconjugacy threshold below which the saccadic system consistently generated pure asymmetric saccades. By definition, these saccades present the entirety of the disconjugacy during the intrasaccadic period, and thus with ratios along the 1:1 line. Above this threshold, the engagement of vergence would have become necessary, as proposed by Bush et al. (1994).

As the time analysis described in the bottom panels in Fig. 9 indicates, this disconjugate response is a true saccadic-generated perisaccadic vergence response driven by an internal disparity adaptive signal. This signal is treated by the vergence system in the same way as a visual disparity. It cannot be the result of a gain modulation of an already existent visually-driven vergence response.
(Munoz et al. 1999), with the primary steps being conjugate: there is no vergence activity to act upon. Midbrain vergence burst cells are silent during conjugate saccades, which carry zero disparity. Furthermore, as Erkelens et al. (1989b) have reported, saccadic disconjugate adaptation, once developed, persists during monocular viewing, where there is also no visual disparity-driven vergence to modulate.

Several studies, among others Seeberger et al. (2002) and Wallman and Fuchs (1998), have demonstrated that version postsaccadic visual errors, and not proprioceptive or efferent copies of the burst commands associated with the visually-driven corrective saccades, drive the version adaptive process. This is likely also true for the vergence-driven component, with the adaptive process using the postsaccadic visual disparity information and not an efferent copy of the corrective vergence response. A cyclopean/disparity dual adaptive mechanism well matches the observation that adapting one eye while the other eye is patched (Albano and Marrero 1995; Snow et al. 1985; Optican and Robinson 1980; Abel et al. 1978) generated conjugate adaptive changes, i.e., equally affecting the patched eye. With no disparity information available due to the patching, only the version adaptation was activated, with the errors in the viewing eye treated, by default, as version errors. Scudder et al. (1998) presented evidence that muscle tenectomy and bi-ocular double step saccadic paradigms most likely engage the same version adaptive mechanism.

It is possible that, in the long-term, a true asymmetric monocular recalibration may take over by utilizing the short-term corrections as a guide. There is indication that short-term and long-term saccadic version adaptation rely on different mechanisms (Robinson et al. 2006). Using an adaptive bi-ocular paradigm and blindfolding the animals between the daily sessions, the authors observed that when a new version adaptive challenge was introduced after allowing the animal to long-term adapt to the previous challenge, the animal presented a normal short-term amount of version adaptation, as if the previous challenge was, with time, transformed into a new baseline. If too little time was allowed
to pass between challenges, the adaptation to the previous challenge significantly reduced the next one. Small lesions of the cerebellar oculomotor vermis impaired short-term version adaptation, but long-term recovery was still present (Barash et al. 1999).

Why should the saccadic system need to rely on the vergence system to adaptively maintain binocular alignment when there is substantial evidence that the saccadic system, during 3-D transfers of gaze, can generate different commands to the two eyes (for a review see Cullen and Van Horn 2011 and King 2011), with resulting intrasaccadic vergence changes much larger than our adaptive vergence goals of 2°? We entertain the possibility that disconjugate saccades, whether visually-driven, aniseikonic, or short-term adaptive, can only occur when there is an ongoing smooth vergence response, i.e., they are the result of vergence-saccadic interactions at the immediate premotor level, with the saccadic system, otherwise, set to be strictly conjugate by long-term monocular recalibrations. Thus, during uni-ocular and symmetric short-term adaptation, the saccadic system is forced to generate its own disparity signal, which then activates the vergence system, in order to control its binocular alignment. Monocular asymmetric saccadic contributions (Cullen and Van Horn 2011) and/or intrasaccadic vergence enhancements (Erkelens 2011; Busettini and Mays 2005b; Zee et al. 1992), elicited as the result of downstream saccadic-vergence interactions, are added to the ongoing smooth vergence response, which we unmasked with our $PO_{[0-50]}$ measures in both control and adaptive sets. Busettini and Mays (2005b) found that, after the contribution of the smooth vergence component is subtracted, the amount of intrasaccadic asymmetry was linked to the vergence motor error at the time of the saccade and not to the initial visual goal of the movement. Erkelens (2011) suggested a multiplicative interaction between vergence velocity and saccadic burst signals.

An obvious and quite radical consequence of our hypothesis is that short-term adaptive, 3-D visually-driven, or aniseikonic pure asymmetric saccades, i.e., without vergence co-activation, do not exist. A logical explanation for this behavior would be that the saccadic system only has access to cyclopean
information. At the same time, we do expect long-term monocular gain corrections, needed to
maintain long-term saccadic conjugacy when no depth changes are called for. Indirect evidence for
such a long-term mechanism is that the vergence system is silent during conjugate saccades (Mays et
al. 1986; Judge and Cumming 1986) indicating that there are no long-term vergence-driven
corrections of saccadic binocular misalignments. We consider it quite unlikely that all the midbrain
vergence cells reported in the literature are from animals with perfectly balanced saccadic signals to
the two eyes. This long-term adaptive mechanism would make, paradoxically, conjugate saccades the
only true pure asymmetric saccades, in the sense that their conjugacy is the result of different long-
term adaptive commands to the two eyes which do not require vergence co-activation.

Although we are well aware that this is a novel idea on which much further work is needed,
strong evidence for this hypothesis is that saccades elicited by stimulation of the superior colliculus
(SC) are, in the absence of an ongoing vergence, always strictly conjugate. Evident intrasaccadic
asymmetries occurred only when the SC stimulation was delivered during an ongoing disparity-driven
smooth vergence eye movement (Chaturvedi and van Gisbergen 1999). There is no evidence for
coding of asymmetric saccades at the level of the SC during 3-D gaze transfers (Walton and Mays
2003), suggesting that any vergence-saccadic interaction occurs further downstream, at the level of
the midbrain vergence burst neurons and/or the saccadic long-lead and short-lead burst neurons, with
the SC inherently a conjugate structure. Unfortunately, most of the studies describing the effects of
partial lesions of the SC or of stimulation or lesions in the downstream structures, including saccadic-
related cerebellar areas, used only one eye coil, and, consequently, measures of saccadic conjugacy
during these experiments were not taken. A recent work, using binocular recordings, reported that
stimulation in some locations inside the monkey central mesencephalic reticular formation generated
asymmetric saccades (Waitzman et al. 2008). The closeness of this region to the supraoculomotor
area, where vergence cells are located (Mays et al. 1986; Judge and Cumming 1986; Mays 1984),

40
makes these stimulation results, as pointed out by the authors, somewhat problematic, and most conclusions about a monocular saccadic encoding in this region were derived from recordings while the animal executed 3-D gaze transfers, and therefore when the vergence system was also active. This observation also applies to all other studies reporting monocular saccadic encoding (Cullen and van Horn 2011; King 2011).

In the past, the strongest criticism for the asymmetry of a pure asymmetric saccade, i.e., with no visible pre or postsaccadic smooth vergence responses, to be vergence-driven, directly or indirectly by vergence modulating the asymmetry of the saccadic bursts in the two eyes, was that the vergence system was seen as a “smooth”, i.e., slow system, and with a long-delay visual feedback loop (Rashbass and Westheimer 1961). The dual model of the vergence system (Hung et al. 1986) also has the final reaching of the goal controlled by visual feedback. Following this reasoning, due to its slow dynamics and low gain needed to maintain stability, and the time delay in the visual detection of the goal being already reached inside the very short duration of the saccade, any intrasaccadic disparity-driven smooth vergence response would have had necessarily extended in time well beyond the end of the saccade. Thus, not surprisingly, these saccades were automatically attributed to a monocular saccadic mechanism. The evidence, initially proposed by Zee et al. (1992), and confirmed by Busettini and Mays (2005b), of the existence of a rapid vergence local feedback loop similar to the one proposed for saccades has greatly weakened this criticism. In this schema, an internal rapid estimate of the progress of the vergence response allows for a saccadic-like, non-visual correction of the vergence motor error driving the vergence response. It is important to observe that this evidence implies that any monocular contribution also has to be delivered to the vergence local feedback loop, in order to properly adjust the post-saccadic smooth vergence response to avoid overshooting. Thus, the lack of pre and postsaccadic smooth vergence is not, necessarily, evidence of no vergence co-activation during the intrasaccadic period, as it was generally assumed.
Comparisons with previous studies

Bi-ocular double step saccadic paradigms applied to macaques are reported in Albano and King (1989) and Straube et al. (1997a), together with studies aimed at the determination of the ability of the adaptive process to adjust for context and to transfer to other saccades (Noto et al. 1999; Watanabe et al. 2000; Tian and Zee 2010). The paradigm used in the Albano and King study (1989) was a bi-ocular pseudo-random task, but with each saccade starting straight ahead and with the secondary step a fraction of the saccadic size, not of the primary target step. The paradigm used in Straube et al. (1997a) was practically identical to our bi-ocular pseudo-random task, and the results were similar to ours in terms of adaptive constants, amount of adaptation, and $R^2$. Increasing gain presented a longer adaptive constant (their average value 1178 saccades for a 30% increase) than decreasing gain (368). As for our data, the variability between the daily sessions was significant. Their attempt to quantify the dynamics of the adapted saccades was also mostly inconclusive, varying between animals, although for the 50% gain reduction there was indication, for the most reduced saccades, of further slowdown compared to similarly “fatigued” saccades. The postsaccadic behavior was not quantified. Our study is the first with a systematic comparison between fully-predictive and pseudo-random designs, both reported in studies with humans, but never together. We found that the simpler, in terms of setup and data analysis, fully-predictive design gave very similar results, with prediction playing a very minor role.

We are not aware of uni-ocular or symmetric studies using the double step saccadic paradigm in monkeys. Oohira and Zee (1992) had normal monkeys wearing laterally-displacing prisms in front of one eye for several days. Interestingly, even after 15 days of wearing the prism, 2.3° convergence disconjugacies were achieved with a still significant postsaccadic component in the patched eye during their monocular controls (their Fig. 3). For 2.3° divergence deviations, the correction was mostly intrasaccadic (their Fig. 2). Viirre et al. (1988) used surgical alterations in one horizontal
rectus muscle (in some animals the medial rectus, in others the lateral rectus) to elicit disconjugate misalignments. After the operated eye was kept patched for 7 days following surgery, the patch was taken off and, after one week, 5 of the 8 animals had a good recovery of function. The animal with the largest eye deviations failed to recover. Two other animals, albeit with deviations in the same range of 3 animals which recovered, did not. Unfortunately, no data are available regarding the ability of the animals that failed to recover to short-term adapt prior to surgery, or if they presented binocular sensory or motor abnormalities.

Neural substrate

Very little is known about the neural substrate of saccadic adaptation to uni-ocular and symmetric gain alterations, and if it is monocularly or binocularly organized. Cerebellum, superior colliculus, and the vergence supraoculomotor and dorsal areas are the most obvious targets for single unit recordings during uni-ocular and symmetric adaptive paradigms. A detailed review of the extensive literature regarding version adaptation and its neural substrate can be found in Hopp and Fuchs (2004).

CEREBELLUM. Cerebellum plays an important role in vergence and accommodation (Gamlin et al. 1996), as is evident in patients with cerebellar lesions (Sander et al. 2009). It is the most logical location to search for the generator of the adaptive vergence signal unmasked by our study. Several of the cerebellar areas described below are also associated with saccadic eye movements. May et al. (1992) have reported that the fastigial and interpositus nuclei of the cerebellum have reciprocal connections with the supraoculomotor area (SOA), the main premotor vergence area. Little is known about the function of the fastigial nucleus in vergence or accommodation, although Zhang and Gamlin (1996) found, in the posterior region of this nucleus, cells related to vergence and accommodation. Stimulation of the fastigial oculomotor region (FOR) elicited, depending on the location of the electrode, ipsiversive or contraversive saccades (Noda et al. 1988). The caudal fastigial nucleus
presented modifications in its firing consistent with this area being involved in version saccadic adaptation (Scudder and McGee 2003; Inaba et al. 2003). Its direct connections with the oculomotor brainstem make this area the main relay of the adaptive version signals (Noda et al. 1990). The posterior interposed nucleus presents cells related to divergence and relaxation of accommodation and insensitive to conjugate saccades (Zhang and Gamlin 1998), as well as cells with activity mostly related to vertical saccades (Robinson 2000), but its contribution to adaptive processes, if any, is unknown. 

Although conjugacy is most likely controlled by the cerebellum, the only evidence for this is a report by Takagi et al. (2003) showing that lesions of the dorsal cerebellar vermis affect both binocular alignment and disconjugate prism adaptation. This observation is consistent with preliminary results by Gamlin and Zhang (1996) that muscimol lesions in the posterior portion of the fastigial nucleus, which receives input from the dorsal cerebellar vermis, caused vergence abnormalities. Patients with cerebellar dysfunctions show both conjugate dysmetria and deficits in binocular alignment (Versino et al. 1996). These authors suggested that the flocculus and paraflocculus might be in charge of calibrating the yoking of the eyes and both conjugate (Optican et al. 1986) and disconjugate postsaccadic drifts. These areas are known to be involved with vestibular adaptation (Anzai et al. 2010; Nagao and Kitazawa 2003; Rambold et al. 2002). Total cerebellectomy in monkeys completely abolished adaptive reaction of the animal to the saccadic dysmetria and postsaccadic drifts elicited by tenectomy in the recti muscles of one eye (Optican and Robinson 1980). These animals presented long-term uncompensated saccadic hypermetria and post-saccadic drifts. Animals with partial midline cerebellar lesions affecting the vermis, paravermis, and fastigial nuclei, but not the floccular area, continued to present saccadic dysmetria but were able to reduce the postsaccadic drifts. Conversely, floccular lesions alone preserved the capability to eliminate the dysmetria, but the animal was not able to eliminate the postsaccadic drifts (Optican et al. 1986).
Nitta et al. (2008) have observed cells in the dorsal vermis with activity related to vergence and fronto-parallel pursuit. A number of reports confirmed that lesions of the lobules VIc and VII of the cerebellar vermis – commonly termed the oculomotor vermis (OV) – abolished the ability of monkeys to compensate for saccadic dysmetria surgically induced by tenectomy (Optican and Robinson 1980) or by bi-ocular double-step saccadic paradigms (Barash et al. 1999). Analysis of the simple spike activity (Kojima et al. 2010) and of the complex spike activity (Soetedjo et al. 2008) of Purkinje cells in the OV support the involvement of this area in version saccadic adaptation. Pharmacological inactivation and disinhibition seem to indicate that each OV controls the metrics of ipsiversive saccades, with no consistent effects on contraversive saccades. Unfortunately, all these studies recorded the movement of only one eye. As noted earlier, binocular recordings suggest that OV is also related to convergence and the maintenance of binocular alignment.

The precerebellar nucleus reticularis tegmenti pontis (NRTP) is an important relay of SC activity (Harting 1977) to the oculomotor vermis (Brodal 1980), and it would be logical to expect NRTP to be unaffected by saccadic adaptation, being located upstream of the main cerebellar adaptive centers. Surprisingly, changes in the firing behavior during bi-ocular saccadic adaptation were found to be present already at the level of NRTP (Takeichi et al. 2005). The authors proposed the existence, in addition to the known connection between NRTP and OC, of a feedback connection from the caudal fastigial nucleus, which receives direct inputs from the OC (Noda et al. 1990). NRTP is involved in several oculomotor functions, including stabilization of Listing’s plane (Van Opstal et al. 1996), vergence (Gamlin and Clarke 1995), smooth pursuit (Suzuki et al. 2003), and eye-head gaze pursuit (Suzuki et al. 2009). Its multimodality and its inputs from cortical areas that carry in-depth information (frontal eye field: Stanton et al. 1988a,b; Huerta et al. 1986; supplementary eye field: Shook et al. 1990), makes NRTP one of the most likely candidates for the encoding of the adaptive disparity signal.
SUPERIOR COLLICULUS. With regard to bi-ocular adaptation, Quessy et al. (2010) found that the locus of activity in the motor map at the level of the deep layers of the SC did not change during adaptation, which is consistent with a downstream gain recalibrating mechanism. Frens and van Opstal (1997) reported similar conclusions. On the contrary, Takeichi et al. (2007) found changes in SC firing consistent with the SC being the site of the adaptation or at least receiving signals related to it, although if, as proposed by Soetedjo et al. (2002) and others, the SC is inside the saccadic local feedback loop, modifications downstream would likely be mirrored in the SC firing. Saccades are preceded by a shift of the focus of visual attention. Ditterich et al. (2000) did not see changes in the metrics of the shift of attention after adaptation, which is consistent with a premotor gain correction and not a visual remapping.

The stimulation results from the study of Chaturvedi and van Gisbergen (1999) and the behavior of the SC during 3-D transfers of gaze (Walton and Mays 2003) do not support the hypothesis of involvement of the SC in the generation of visually-driven asymmetric saccades nor uni-ocular and symmetric saccadic adaptation. Walton and Mays (2003) reported that an ongoing vergence affected the SC, but in an unspecific way not consistent with monocular encoding. It would be of some interest to verify if the vergence adaptive component also modifies the SC activity. The evidence of neural activity related to smooth-pursuit in the rostral area of the SC (Krauzlis et al. 2000; Krauzlis 2001) suggests an involvement of the SC beyond just saccades. In the cat, the rostral SC is related to accommodation (Sawa and Ohtsuka 1994) and vergence (Suzuki et al. 2004), and the visual layers of the SC present disparity sensitivity (Mimeault et al. 2004), but these properties do not seem to be present in the primate SC.

VERGENCE SUPRAOCULOMOTOR AND DORSAL AREAS. Two groups of vergence cells have been described in the monkey midbrain. One group of these midbrain vergence-related cells is localized in the mesencephalic reticular formation just above the oculomotor nucleus (Mays et al.
1986; Judge and Cumming 1986; Zhang et al. 1991; Zhang et al. 1992), and is so named the supraoculomotor area (SOA). The second group is located just slightly more superficially (Mays et al. 1986), in front of the SC. This is often termed the dorsal area. There is no known difference in behavior when comparing SOA and dorsal groups, although their target neurons and source of inputs are likely different. Both contain convergence and divergence neurons, with some cells firing only during the phasic part of the response (burst cells) and others presenting a tonic firing related to the vergence angle (tonic and burst-tonic cells). There is evidence, from antidromic activations, of direct excitatory monosynaptic connections from SOA convergence burst-tonic cells to ipsilateral medial rectus motoneurons (Zhang et al. 1991). Our hypothesis expects these cells to have similar firing patterns during both control and adaptive uni-ocular and symmetric tasks.

Implications for strabismus

Our results, if confirmed by single unit recordings, have evident impact on the short-term saccadic adaptation of subjects with impaired disparity detection, and perhaps also long-term, if the short-term saccadic-controlled but vergence-driven adaptation is the needed first step in guiding the long-term adaptive process. During patching experiments, Das et al. (2004) found that the conjugate transfer of adaptation to the non-viewing eye, while adapting the viewing eye using a double-step adaptive saccadic task, is preserved in monkeys with very large sensory-induced strabismus. These animals, tested monocularly, presented disconjugacy in their saccadic eye movements and postsaccadic drifts (Fu et al. 2007), but their version adaptive mechanism was apparently still functional. No data are available on whether these animals had a normal AC/A ratio, i.e., the relative amount of vergence elicited by an accommodative stimulus applied to one eye while patching the other eye. A normal AC/A ratio would indicate that these animals have a functional vergence system from a motor point of view even if, of course, they had no disparity sensitivity whatsoever, having never experienced binocular vision during their critical developmental period. Interestingly, in the
study by Quick et al. (1994) on natural strabismic animals, the strabismic animal that experienced bilateral retinal hemorrhage at birth (INDUCED animal), and therefore probably presenting a sensory-induced strabismus, had a normal AC/A ratio. With these animals unable to detect postsaccadic disparity errors, and therefore unable to engage the vergence-driven disconjugate adaptive process, their binocular misalignment might just be their vergence-driven adaptive default value.

ENDNOTES

1. There is indirect evidence, supported by the presence of small rapid oscillations in the version trace following the end of the primary saccade, that OPNs in humans might have, sometimes, an extended pause after the primary saccade during combined vergence-saccadic responses. These conjugate oscillations were observed, during combined movements associated with large vergence changes, in approximately 1/3 of the trials and in all the subjects tested (Ramat et al. 1999). Their frequency of occurrence decreased for smaller vergence changes, and they were not observed for conjugate saccades. There were no evident effects on the vergence traces in the trials presenting the conjugate oscillations, suggesting that the delayed resuming of the OPN firing, and, as a consequence, the delayed blocking of the saccadic system after the primary saccade occurring in these trials, had little behavioral impact overall. We had no evidence in our monkey data of such oscillations or of a bimodal behavior in the resumption of the OPN firing (Busettini and Mays 2003).
ACKNOWLEDGEMENTS

We thank S. Hayley for computer programming, Christopher Williams for help in the data analysis, L. Millican and A. Yildirim for technical assistance, and L. Phillips for administrative assistance.

GRANTS

This research was supported by the National Eye Institute, NIH, with grant to Dr. Busettini (ARRA supplement to R01 EY-017283) and Core grant P30 EY-03039 to the UAB Vision Science Research Center, and by The EyeSight Foundation of Alabama with grants to Dr. Busettini FY2006-2007-42 and FY2011-12-274.
FIGURE LEGENDS

FIG. 1. The double-step saccadic paradigms. In the 6 upper panels, the thin dashed lines (LM and RM) are the calibrated feedback signals from the galvanometers indicating the target positions, while the thick solid lines (LE and RE) are the left-eye and right-eye positions. A dichoptic arrangement using matching orthogonal polarizers and a non-depolarizing screen allowed separate presentation of the targets to the two eyes (red traces: left eye; black traces: right eye). The primary target steps were always identical horizontal steps applied to both eyes, 10° rightward steps in the example in the figure. The secondary steps were +20% or -20% of the primary steps, with the exclusion of the symmetric case where they were equally split, in opposite directions, between the two eyes. The top panels illustrate the visual controls, where the secondary steps were delivered with the primary steps. In the bi-ocular control (BC), the secondary steps were identical and in the same direction for the two eyes. In the example, the two same-direction 2° secondary steps generated a rightward 12° single-step trial to both eyes. In the uni-ocular control (UC), the secondary step was applied only to one eye. In the example, with the 2° secondary step added to the right eye, the result is a rightward 10° step on the left eye and a rightward 12° step on the right eye. In binocular coordinates, this translates into a rightward version of 11° and a divergence of 2°. In the symmetric control (SC) example, the 2° step is split, in opposite directions, between the two eyes, to still have a divergence of 2°, but no alteration in version, which remained 10°. The middle panels illustrate the matching adaptive tasks. In these, the animal always saw only the conjugate primary steps, with the secondary steps applied while the animal was responding to the primary steps. The two bottom drawings illustrate the target trajectories on the horizontal meridian plane for the uni-ocular +20% secondary step on the right eye paradigms in the fully-predictive (left) and pseudo-random (right) designs. In both cases the starting position of the target for the next trial was the position achieved at the end of the previous trial. The main difference was that, in the fully-predictive design, a rightward 10° primary target step was always followed by a
leftward 10° and so on, while in the pseudo-random design the primary target step in the next trial could have been, randomly selected, a rightward 5°, a leftward 5°, a rightward 10°, or a leftward 10°. Each paradigm was presented in separate daily sessions in a random sequence, lasting as long as the animal continued to perform the primary saccadic task. Rightward eye movements are reported as positive, leftward movements as negative.

**FIG. 2.** Examples of intrasaccadic version adaptation as a function of trial # in the bi-ocular adaptive paradigms (fully-predictive design) and associated conjugacy tests from animal #1. Panel A illustrates an example of forward bi-ocular secondary steps, which simulate a sudden identical decrease in saccadic gain in both eyes. The animal sees 10° steps in both eyes, but the actual target shift, with the added intrasaccadic second steps, is 12°. The animal gradually adapts by increasing the intrasaccadic version response. Panel B illustrates the case of bi-ocular backward secondary steps, simulating a sudden identical increase in saccadic gain in both eyes. The animal sees 10° steps in both eyes, but the actual target shift, with the added intrasaccadic second steps, is 8°. The animal gradually adapts by decreasing the intrasaccadic version response. Trial # is the number of trials from the start of the adaptive experiment. The initial control trials, in grey, therefore have a negative Trial #. In the fully-predictive design, with alternating rightward and leftward 10° saccades, the number of visual exposures to each of the adaptive trials is ½ of the trial #. The red lines are single adaptive constant exponential fits, with asymptotic amplitude ΔAS and adaptive constant AC. Panels C and D show, for the data in Panels A and B respectively, the relationship between the left-eye intrasaccadic responses and the right-eye intrasaccadic responses. The red line is the linear regression, with SL the slope, reported together with the R².
FIG. 3. Intrasaccadic version gain adaptation as a function of trial # in the bi-ocular adaptive paradigms (fully-predictive design): overall results. Left panel: exponential fits of the primary saccade version gain as a function of trial # for the two bi-ocular adaptive sessions (rw +20% lw +20%; and rw -20% lw -20%) in the fully-predictive design from animal #1. Right panel: from animal #2. lw: leftward primary saccades; rw: rightward primary saccades. The two tables report, for each set, the value of the adaptive constant of the exponential AC together with the value of its asymptotic standard error (ASE) in parenthesis, the % of gain change achieved during the session (Δ), the total number of adaptive trials in the session (TN) and on which the fit was estimated, and the R² of the fit. For the two sets with an asterisk, the single exponential fit did not converge and we used a linear fit with slope Sl. The # in the Δ column indicates that the animal achieved adaptation steady state for that set. For clarity, the panels show the fits truncated at 1500 adaptive trials for the sets with TN>1500.

FIG. 4. Comparison of average version profiles between bi-ocular fully-predictive adaptive and associated control sets. Upper panels: backward adaptive step (animal #1, bi-ocular -20% adaptation, rightward saccades). Lower panels: forward adaptive step (animal #1, bi-ocular +20% adaptation, rightward saccades). Panels BA and FA: average version position (HVS) and version velocity (HVS dù) of the last 50 rightward saccades (continuous lines) of the two adapted sets, with the dotted lines the ±SD. Panel BB: comparison of the version position and velocity averages (AD) from panel BA with the averages of the last fifty 8° (CONT) and 10° (CONT) saccades of the correspondent control session. Panel FB: averages (AD) from panel FA compared with the averages of the last fifty 10° (CONT) and 12° (CONT) saccades of the correspondent control session.

FIG. 5. Extrasaccadic version responses in the bi-ocular fully-predictive adaptive paradigms. Panel A: changes in (PR)esaccadic version position from the onset of the primary 10° target steps to the onset
of the animal’s primary saccade as a function of Trial # (animal #2 bi-ocular -20% adaptation, rightward saccades). 50 initial controls: open grey circles; adaptive responses: open black circles and, near the end of the session, filled grey circles. Panel B: (IN)trasaccadic change in version position. Panel C: changes in version position during the extended postsaccadic period, from primary saccade offset to 600 ms after offset. Panel D: total change in version position, from the onset of the primary target steps to 600 ms after the end of the primary saccade. Panel E: version position profiles and version velocity profiles, synchronized with respect to primary saccade offset, of the last 15 saccades of the session, identified with the filled grey circles in Panels A, B, C, and D. The vertical dotted line identifies the location of the onset of the earliest corrective saccade in the set. Panel F: primary saccade version position change vs. corrective saccade version position change ($R^2=0.76$) for the 15 trials illustrated in panel E.

Fig. 6. Postsaccadic drifts in the bi-ocular fully-predictive paradigms. Upper panels: version velocity average ($\text{HVS} \pm \text{SD}$) of the fifty initial primary-only leftward control saccades (left panel) and of the last fifty leftward downward-adapted saccades of the bi-ocular -20% session (right panel). Magnified inserts (location identified by the blue boxes): horizontal version velocity $\text{HVS}$, horizontal left eye velocity $\text{HL}$, horizontal right eye velocity $\text{HR}$, and vergence velocity $\text{VG}$. Lower panels: upward-adapted (+20%) data. All the traces were synchronized with saccade end prior to averaging. Animal #1, fully-predictive design, -20% or +20% bi-ocular adaptive paradigms, leftward saccades.

Fig. 7. Postsaccadic overshoots in the bi-ocular tasks. Panels A and E: changes in horizontal right eye position in the $\text{PO}_{[0,50]}$ interval as a function of trial #. Panels B and F: changes in horizontal left eye position. Panels C and G: changes in vergence position; Panels D and H: changes in horizontal version position. The upper panels report the data for the rightward saccades in the -20% bi-ocular
adaptive fully-predictive session in animal #2. The lower panels report the same measures for the leftward saccades in the same session. The red lines are second-order polynomial fits.

FIG. 8. The postsaccadic overshoots in the bi-ocular paradigms are determined by the saccadic direction and fatigue. Superimposed second order polynomial fits of the changes in version position in the PO\([0-50]\) interval for the four bi-ocular fully-predictive adaptive sets (lw +20%, rw +20%, lw -20%, and rw -20%) and for the associated controls (lw CONT and rw CONT) as function of trial #. Left panel: animal #1. Right panel: animal #2.

FIG. 9. Single-trial examples from a uni-ocular fully-predictive design adaptive paradigm, and test of the vergence adaptation/prediction hypothesis. Upper panels: eye positions (left eye LE, right eye RE, vergence VG) and calibrated feedback signals from the mirrors (left eye mirror LT, right eye mirror RT). Middle panels: eye velocities. Panel A: an initial 10° primary-only control trial. Panel B: an early adaptive trial, with the disparity landing error entirely compensated by a postsaccadic visually-driven smooth vergence response. Panel C: a late adaptive trial, presenting a large postsaccadic component (arrow). Some presaccadic vergence response is also present (asterisk). Note that the entire disparity error in this late trial is compensated perisaccadically, with no need for a later visually-driven corrective smooth vergence response. These panels report the time intervals used in the analysis as vertical dashed lines, and are labeled in panel C. The vergence velocity traces (\(\dot{VG}\)) in the middle panels are amplified 5 times with respect to the right-eye and left-eye velocity traces for clarity. Trials from animal #1, +20% uni-ocular step on the right eye (crossed disparity), leftward saccades. The lower panels plot the changes in vergence position in the \(IN, PO_{[0-50]}, VIS_{[0-100]},\) and \(VIS_{[100-200]}\) intervals as a function of Trial # for the animal #2 +20% uni-ocular step on the left eye (crossed disparity) rightward saccades.
FIG. 10. Immediate postsaccadic profiles in the fully-predictive uni-ocular paradigms. Layout similar to Fig. 6, with the dashed ±SD of the HVS traces replaced by the HL (red) and HR (green) averages. Upper section: averages of the velocity profiles, after alignment with saccadic offset, of the initial fifty rightward 10° primary-only saccades (left panels) and of the last fifty rightward adapted saccades (right panels) in the two uni-ocular fully-predictive rightward saccades convergence sets (-20% secondary step on the right eye, and +20% secondary step on the left eye) in animal #1. Lower section: same averages from the two uni-ocular fully-predictive rightward saccades divergence sets (+20% secondary step on the right eye, and -20% secondary step on the left eye) in animal #1.

FIG. 11. Version adaptive components in the uni-ocular fully-predictive tasks. Panel A: single-trial change in horizontal version position in the PO [0-50] interval for the leftward saccades in the +20% uni-ocular step on the right eye task for animal #2. Panel C: same measure for rightward saccades for the -20% uni-ocular step on the right eye task. Red lines are second order polynomial fits, which are reported in Panels B and D for all 4 uni-ocular sets with that saccadic direction. Lower panels (similar layout): version changes in the IN time interval for the same sets in the upper section. Red lines are single-exponential or linear fits, reported in Panels F and H as version primary gain fits (1=10°) for all 4 uni-ocular sets with that saccadic direction.

FIG. 12. Sample comparisons of vergence position and velocity profiles in a uni-ocular fully-predictive set. First column: initial fifty primary-only controls of the control paradigm. Second column: last fifty same-saccadic-direction trials of the same control set. Third column: initial fifty primary-only controls of the associated adaptive paradigm. Fourth column: last fifty same-saccadic-direction trials of the same adaptive set. The single vergence position traces are in black, and the single vergence velocity traces are in red. The same single-trial data are also plotted as averages in the
row below, with in red the average vergence velocity and the green lines the ±SD. The black solid line is the average vergence position, and the dotted profile is the average version velocity trace. Both the single-trial vergence positions traces (as a group to maintain the original scatter) and the position averages were offset with respect to their actual values to not superimpose on the velocity traces for clarity. Upper half: uni-ocular +20% with the step on the left eye fully-predictive set, rightward saccades. Lower half: leftward saccades. From animal #1.

Fig. 13. Vergence adaptive components in the uni-ocular fully-predictive paradigms. Single-trial measures from two convergence and two divergence sets from animal #2, with the secondary steps applied to one or the other eye. First column: changes in vergence position inside the IN interval as a function of trial #. Second column: inside the PO[0-50] interval. Third column: inside the PREVISUAL interval. Fourth column: IN change in vergence as a function of PREVISUAL change, with the dashed line indicating PREVISUAL changes entirely contained inside the intrasaccadic period. The arrows illustrate the direction of the adaptive process. In the first three columns the red lines are single adaptive constant exponentials, while the red lines in the fourth column are second order polynomial fits. For clarity, the y-scale factor for the PO[0-50] data is twice as large with respect to the IN and PREVISUAL panels, and plots of sets with more than 1500 adaptive trials are truncated at 1500, although the fits were computed using the entire set.

FIG. 14. Change in vergence position in the uni-ocular and symmetric adaptive paradigms inside the PREVISUAL interval as a function of trial #: overall results. Left panel: single adaptive exponential or linear fits of the vergence change in the PREVISUAL time interval as a function of trial # for the four uni-ocular adaptive sessions (rw L+20% lw L+20%; rw L-20% lw L-20%; rw R+20% lw R+20%; and rw R-20% lw R-20%) in the fully-predictive design from animal #1. Right panel: from
animal #2. Color coding is used to identify the pairs. Top tables: time course measures for the same tasks, with the same layout and symbols used in Figs. 4 and 5. Bottom tables: measures for the two symmetric fully-predictive paradigms (rw D(ivergence) 20% lw C(onvergence) 20%; rw C(onvergence) 20% lw D(ivergence) 20%).

FIG. 15. Sample comparisons of relative contributions of the intrasaccadic vergence response to the overall previsual vergence response between control and adaptive sets. Second order polynomial fits of the vergence position change in the IN(trasaccadic) interval as a function of the vergence position change in the PREVISUAL interval (similar to Fig. 13 fourth column) for all uni-ocular fully predictive adaptive (in color) and associated control (grey) sets. Left panels: convergence sets. Right panels: divergence sets. Upper half: animal #1. Lower half: animal #2. The arrows illustrate the direction of the adaptive process.

FIG. 16. Pseudo-random design: overall results. Top panels and table immediately below, with identical layout and symbols of Fig. 3: intrasaccadic version change as a function of trial # in the pseudo-random bi-ocular adaptive paradigms. Left panel: single adaptive constant exponential or linear fits of the primary saccadic gain as a function of trial # for the four bi-ocular adaptive sessions (rw +20% lw +20%; rw +20% lw -20%; rw -20% lw +20%; and rw -20% lw -20%) from animal #1. Right panel: from animal #2. Color coding is used to identify the pairs. The slope for the lw +20% matched with the rw -20% (black pair) in animal #2 was not significant, and is reported in grey. The bottom tables quantify the PREVISUAL vergence change as a function of trial # for the pseudo-random uni-ocular adaptive paradigms, left table for animal #1, and right table for animal #2. Same layout of tables in Fig. 14.


BI-OCULAR CONTROL (BC)  UNI-OCULAR CONTROL (UC)  SYMMETRIC CONTROL (SC)

BI-OCULAR ADAPTATION (BA)  UNI-OCULAR ADAPTATION (UA)  SYMMETRIC ADAPTATION (SA)

FULLY-PREDICTIVE PARADIGM  PSEUDO-RANDOM PARADIGM

FIGURE 1
BI-OCULAR PARADIGM - FULLY-PREDICTIVE DESIGN
ADAPTATION TIME COURSE AND CONJUGACY

FIGURE 2
BI-Ocular Paradigm - Fully-Predictive Design

Adaptive Constants

**FIGURE 3**

<table>
<thead>
<tr>
<th>Animal #1</th>
<th>Animal #2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>set</strong></td>
<td>Ac or Sl (ASE)</td>
</tr>
<tr>
<td>lw +20%</td>
<td>943 (301)</td>
</tr>
<tr>
<td>rw +20%</td>
<td>363 (65)</td>
</tr>
<tr>
<td>lw -20%</td>
<td>226 (29)</td>
</tr>
<tr>
<td>rw -20%</td>
<td>196 (25)</td>
</tr>
</tbody>
</table>

| **set**   | Ac or Sl (ASE) | Δ (%)  | TN   | R²  |
| lw +20%*  | 0.000081 (0.000015) | +6.7   | 830  | 0.10|
| rw +20%*  | 0.000105 (0.000015) | +8.7   | 830  | 0.18|
| lw -20%   | 381 (55)      | -14.7* | 1564 | 0.34|
| rw -20%   | 207 (35)      | -14.1* | 1564 | 0.21|
BI-OCCULAR PARADIGM - FULLY-PREDICTIVE DESIGN

SACCADIC DYNAMICS

BACKWARD STEP

BA  

BB

FORWARD STEP

FA  

FB

FIGURE 4
FIGURE 5

BI-Ocular Paradigm - Fully-Predictive Design
Extrasaccadic Components

A) Presaccadic version change (°)
B) Intracocular version change (°)
C) Postsaccadic (0-600 ms) version change (°)
D) Total version change (°)
E) Version position profiles
F) Corrective saccade version change (°)
BI-OCULAR PARADIGM - FULLY-PREDICTIVE DESIGN
POSTSACCADIC DRIFTS

FIGURE 6
BI-OCCULAR PARADIGM - FULLY-PREDICTIVE DESIGN
POSTSACCADIC DRIFTS PO\([0-50]\) VALUES

RIGHTWARD SACCADENCES

E  \(R^2 = 0.11\)  F  \(R^2 = 0.48\)  G  \(R^2 = 0.15\)  H  \(R^2 = 0.42\)

LEFTWARD SACCADENCES

A  \(R^2 = 0.11\)  B  \(R^2 = 0.23\)  C  \(R^2 = 0.01\)  D  \(R^2 = 0.27\)

FIGURE 7
BI-OCCULAR PARADIGM - FULLY-PREDICTIVE DESIGN
POSTSACCADIC VERSION DRIFTS PO\(_{[0-50]}\) FITS

FIGURE 8
Figure 9

UNI-OCULAR PARADIGM - FULLY-PREDICTIVE DESIGN
SINGLE TRIALS AND DEVELOPMENT OF DISCONJUGACY

A

B

C

IN

PO[0-50]

VIS[0-100]

VIS[100-200]
FIGURE 10
UNI-OCULAR PARADIGM - FULLY-PREDICTIVE DESIGN
VERGENCE DYNAMICS

CONTROL PARADIGM
10° conjugate controls last fifty visual

ADAPTIVE PARADIGM
10° conjugate controls last fifty adaptive

UNI-OCULAR ON LEFT EYE +20%
RIGHTWARD PRIMARY SACCADIES

UNI-OCULAR ON LEFT EYE +20%
LEFTWARD PRIMARY SACCADIES

FIGURE 12
FIGURE 13
ADAPTIVE CONSTANTS
UNI-OCULAR PARADIGM - FULLY-PREDICTIVE DESIGN

SYMmetric PARADIGM - FULLY PREDICTIVE DESIGN
UNI-OCULAR PARADIGM - FULLY-PREDICTIVE DESIGN
RELATIVE POSTSACCADIC VERGENCE CONTRIBUTION

FIGURE 15
ADAPTIVE CONSTANTS

BI-OCCULAR PARADIGM - PSEUDO-RANDOM DESIGN

Animal #1

![Graph showing version gain primary saccade](image)

<table>
<thead>
<tr>
<th>set</th>
<th>Ac or S (ASE)</th>
<th>Δ (%)</th>
<th>TN</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>lw +20%</td>
<td>0.000046 (0.000008)</td>
<td>8.8</td>
<td>1921</td>
<td>0.09</td>
</tr>
<tr>
<td>rw +20%</td>
<td>0.000047 (0.000007)</td>
<td>9.0</td>
<td>1921</td>
<td>0.14</td>
</tr>
<tr>
<td>lw -20%</td>
<td>254 (52)</td>
<td>-20.5</td>
<td>969</td>
<td>0.60</td>
</tr>
<tr>
<td>rw -20%</td>
<td>370 (95)</td>
<td>-15.0</td>
<td>969</td>
<td>0.59</td>
</tr>
<tr>
<td>lw +20%</td>
<td>248 (104)</td>
<td>9.0</td>
<td>994</td>
<td>0.24</td>
</tr>
<tr>
<td>rw -20%</td>
<td>255 (48)</td>
<td>-15.6</td>
<td>994</td>
<td>0.50</td>
</tr>
<tr>
<td>lw -20%</td>
<td>247 (41)</td>
<td>-19.2</td>
<td>1807</td>
<td>0.31</td>
</tr>
<tr>
<td>rw +20%</td>
<td>593 (282)</td>
<td>11.9</td>
<td>1807</td>
<td>0.19</td>
</tr>
</tbody>
</table>

Animal #2

<table>
<thead>
<tr>
<th>set</th>
<th>Ac or S (ASE)</th>
<th>Δ (%)</th>
<th>TN</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>lw +20%</td>
<td>0.000032 (0.000026)</td>
<td>2.4</td>
<td>760</td>
<td>0.01</td>
</tr>
<tr>
<td>rw -20%</td>
<td>0.000066 (0.000007)</td>
<td>9.4</td>
<td>1430</td>
<td>0.34</td>
</tr>
</tbody>
</table>

UNI-OCCULAR PARADIGM - PSEUDO-RANDOM DESIGN

Animal #1

<table>
<thead>
<tr>
<th>set</th>
<th>Ac or S (ASE)</th>
<th>Δ (%)</th>
<th>TN</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>lw L+20%</td>
<td>430 (180)</td>
<td>-1.0</td>
<td>902</td>
<td>0.43</td>
</tr>
<tr>
<td>rw L+20%</td>
<td>385 (84)</td>
<td>0.9</td>
<td>902</td>
<td>0.62</td>
</tr>
<tr>
<td>lw L-20%</td>
<td>486 (112)</td>
<td>0.9</td>
<td>1378</td>
<td>0.45</td>
</tr>
<tr>
<td>rw L-20%</td>
<td>919 (437)</td>
<td>-1.0</td>
<td>1378</td>
<td>0.38</td>
</tr>
<tr>
<td>lw R+20%</td>
<td>749 (117)</td>
<td>1.4</td>
<td>1961</td>
<td>0.60</td>
</tr>
<tr>
<td>rw R+20%</td>
<td>387 (91)</td>
<td>-1.0</td>
<td>1961</td>
<td>0.32</td>
</tr>
<tr>
<td>lw R-20%</td>
<td>-0.00047 (0.00004)</td>
<td>-0.8</td>
<td>1714</td>
<td>0.32</td>
</tr>
<tr>
<td>rw R-20%</td>
<td>572 (120)</td>
<td>1.3</td>
<td>1714</td>
<td>0.47</td>
</tr>
</tbody>
</table>

Animal #2

<table>
<thead>
<tr>
<th>set</th>
<th>Ac or S (ASE)</th>
<th>Δ (%)</th>
<th>TN</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>lw L+20%</td>
<td>203 (47)</td>
<td>-1.2</td>
<td>1293</td>
<td>0.32</td>
</tr>
<tr>
<td>rw L+20%</td>
<td>392 (55)</td>
<td>1.6</td>
<td>1293</td>
<td>0.69</td>
</tr>
<tr>
<td>lw L-20%</td>
<td>486 (158)</td>
<td>1.3</td>
<td>1077</td>
<td>0.44</td>
</tr>
<tr>
<td>rw L-20%</td>
<td>-0.00050 (0.00009)</td>
<td>-0.5</td>
<td>1077</td>
<td>0.13</td>
</tr>
<tr>
<td>lw R+20%</td>
<td>123 (54)</td>
<td>0.7</td>
<td>1029</td>
<td>0.21</td>
</tr>
<tr>
<td>rw R+20%</td>
<td>165 (116)</td>
<td>-0.4</td>
<td>1029</td>
<td>0.10</td>
</tr>
<tr>
<td>lw R-20%</td>
<td>980 (470)</td>
<td>-1.2</td>
<td>1132</td>
<td>0.34</td>
</tr>
<tr>
<td>rw R-20%</td>
<td>542 (186)</td>
<td>1.8</td>
<td>1132</td>
<td>0.52</td>
</tr>
</tbody>
</table>

FIGURE 16