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RESEARCH ARTICLE

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Disconjugate memory-guided saccades to disparate targets: evidence for 3D sensitivity

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Abstract The saccadic system has been traditionally regarded as two-dimensional (horizontal, vertical) and basically conjugate in the two eyes. However, saccades to disparate targets (e.g., targets in real three-dimensional space that are located in different directions and at different distances) are naturally disconjugate. We report here that memory-guided saccades to a disparate target flashed 1 s earlier become disconjugate following repeated trials. After 15 min of repetition, the disconjugacy persists even when the target to be remembered is no longer disparate. This suggests fast memory-based learning. Learning, however, fails to occur if, during the repetition trials, the memory delay is 2 s. These findings suggest that the saccadic system has access to a 3D representation of targets and is gifted with 3D short-term memory and learning capacity.

Key words Saccades · Disconjugacy · Disparity · Memory · Associative learning

Introduction

When looking between distant targets (effectively at infinity), saccades are usually conjugate in the two eyes except for a small, transient divergent disconjugacy (see Kapoula et al. 1986; Collewijn et al. 1988; Zee et al. 1992). They are believed to obey Hering's law of equal innervation. Evidence for a structural basis for Hering's law exists for both horizontal and vertical saccades (for a review, see Moschovakis et al. 1996). Conjugacy allows for the image of a fixated object to fall to corresponding retinal points and thus to obtain single binocular vision. Hering's law is mutable, however. Thus, disconjugacy appears if the target is disparate for the two eyes. During exploration of the natural 3D visual world, we commonly shift our gaze among targets that differ both in direction and in depth. Such targets contain disparity (difference between the actual and the target vergence angle). Saccades to targets in 3D space are naturally disconjugate (e.g., Enright 1984, 1992; Erkelens et al. 1989; Zee et al. 1992). Disconjugacy reduces the disparity and allows one to obtain rapidly binocular vision of the new fixated target.

Another common situation requiring disconjugate saccades is optical aniseikonia/image-size inequality. Persons wearing spectacles of different refractive power for the two eyes are exposed to image-size inequality. Aniseikonia creates a distribution of disparity, which simulates a tilt in depth of the surface of targets, even though subjects do not perceive such tilt; at least, subjects who wear anisometropic spectacles for a long period. For instance, if the right-eye image is larger and a target is presented to the right, the plane of binocular fixation of the target is beyond the physical surface of targets; this calls for a divergent saccade. When a target is presented to the left, the plane of its binocular fixation is closer than the physical surface of targets, calling for a convergent saccade.

Since 1950, Ogle described the need for disconjugate saccades in order to obtain rapidly binocular fixation of aniseikonic targets. That saccades indeed become disconjugate was demonstrated only recently in monkeys (Bush et al. 1994) as well as humans (Schor et al. 1990; Lemij and Collewijn 1991; Kapoula et al. 1995; Van der Steen and Bruno 1995). For intermediate or far-viewing distances studied in humans, the disconjugacy develops within a short training period of 3–12 min (Kapoula et al. 1995; Van der Steen and Bruno 1995). Interestingly, after a short training period, saccades remain disconjugate even

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under monocular viewing (in the absence of disparity). Such persistence indicates fast learning.

The mechanisms underlying this fast learning are not well known. Bruno et al. (1995) proposed a parametric readjustment of the saccadic system stimulated by the detection of consistent disparity error after the saccade. Kapoula et al. (1995) observed that the disconjugacy, induced in their study, did not show the typical characteristics of an adaptive mechanism based on progressive reduction of an error signal: the disconjugacy did not increase continuously over time, and it was not always correlated with the amplitude of the saccade. Thus, they proposed a high-level associative learning mechanism based on short-term memory. Pairing of saccades with peripheral retinal disparity would rapidly lead to an association between the saccade and a fast disparity-reducing disconjugacy command. Once linked, the saccade itself triggers the disconjugacy command; thus, saccade-amplitude inequality could be produced even in the absence of disparity (monocular viewing). Fast disconjugacy can be generated either by the saccadic system itself (non-Hering's law saccades) or by a saccade-vergence interaction circuit in the brainstem capable of producing saccade-like vergence movement (see Zee et al. 1992).

The goal of the present study was to test the idea of learning based on short-term memory. We developed a new paradigm, in which subjects made saccades to a remembered target that was aniseikonic and therefore disparate for the two eyes. This was achieved by the use of an afocal magnifier (8%) placed in front of one eye. Each target was presented at the periphery for only 100 ms, and the memory delay (the interval between the offset of the target and the onset of the saccade) was 1 s. The saccade was executed in the dark, and there was no visual feedback afterwards. Subjects could use only peripheral disparity (before the saccade) and only for 100 ms; the disparity had to be memorized until the onset of the saccade. Thus, learning, if any, could only act on the ability to localize and memorize accurately target position in an internal representation of 3D space. This representation should be rearranged on the basis of the distribution of the disparity sensed during the experiment for various target positions to the left and to the right visual periphery. All subjects tested were able to make disconjugate saccades to the remembered disparate target as required by the magnifier. They were able to do so after only 2–8 min of training. After 15 min of training, the disconjugacy persisted even when the target to be remembered was no longer disparate. A summary of these results has been published elsewhere (Kapoula and Bucci 1996).

Materials and methods

Subjects

Eight subjects were tested. They were all normal with no history of strabismus. Their corrected visual acuity was 20/20 in both eyes, and binocular vision was normal (TNO test: 60 s of arc or better). The study was approved by the French Ethics Committee CCPPRB no. 15. Subjects participated in the experiment after giving informed consent.

Induction of aniseikonia

To induce aniseikonia, subjects wore an afocal magnifier of 8% in front of their dominant eye (for five of the six subjects who participated in the first experiment, the right eye was dominant). It should be noted that the magnifier was afocal and had no effect on the accommodation. Thus, this was a reduced situation where disparity was the only cue to depth.

Memory-guided saccade paradigm

In a dark room, subjects were seated 123 cm in front of an egocentric arc of light-emitting diodes (LEDs) positioned horizontally at eye level. The head of the subjects was stabilized with a bite bar (with an individually fitted dental impression of the subject's upper teeth). The subjects fixated a small spot of red light created by the LED (5.6 min of arc). After a variable interval, a target appeared at the periphery at a randomly chosen position to the left or to the right at 5, 10, or 15°. The target was created by illuminating an array of LEDs and was either a normal or a backward letter E 0.4×0.2°. Target letters instead of single dots were used to make the perceptual task more meaningful. Letter recognition is believed to be an automatic process, which occurs even when no response is required. Because of the magnifier, the size of the target and its eccentricity were 8% larger in the eye wearing the magnifier, thereby creating disparity. The target was flashed for only 100 ms. Subjects were instructed to continue to fixate the central dot. After a memory delay of 1 s, the central spot was switched off and the subject was instructed to saccade in complete darkness, as accurately as possible, to the remembered target, which was different in the two eyes. After a period of dark for 1500 ms, the central dot was lit again and the next trial started. There was no visual feedback after the saccade. For the experiments where the magnifier was placed in front of the right eye, the eyes should diverge during rightward saccades and converge during leftward saccades. Subject ST wore the magnifier on the left eye; her eyes should diverge during leftward saccades and converge during rightward saccades.

Eye movement recording

The stimulation and data collection were directed by REX, software developed for real-time experiments and run on a PC. Horizontal saccades from both eyes were recorded simultaneously with a photo-electric device mounted on spectacles (IRIS, SKALAR). The system had an optimal resolution of 2 min of arc, and its range for lateral excursions was up to 30°; its linearity was within 3% for excursions up to 25°. Eye-position signals were low-pass filtered with a cut-off-frequency of 200 Hz and digitized with a 12-bit analogue-to-digital converter. Each channel was sampled at 500 Hz.

Calibration

A preliminary calibration was performed by asking the subjects to fixate back and forth between two stationary targets located at ±20°. Then, subjects performed a standard paradigm of visually-guided saccades: the fixation spot was turned off and the target appeared simultaneously at a randomly selected peripheral position of the arc (5, 10, 15, or 20° to the left or to the right) for 1500 ms. This paradigm was performed twice, under monocular viewing with either eye. Two black curtains mounted on the head support allowed a change from one viewing condition to the other without causing any head motion. Then, the subject performed the memory-guided saccade paradigm in the following conditions.

Testing conditions

Baseline recordings (3 min): memory-guided saccades to non-disparate targets

Viewing was monocular; the target to be remembered was flashed only to the eye wearing the magnifier and, thus, had no disparity. This control condition was used to determine any inherent disconjugacy of memory-guided saccades even when the remembered target did not require disconjugacy.

Training (15 min): memory-guided saccades to aniseikonic disparate targets

Viewing was binocular with the magnifier in front of one eye. Thus, the target to be remembered was disparate in the two eyes. Saccades were recorded continuously.

Post-training recordings (3 min): memory-guided saccades to non-disparate targets

To test for the persistence of learned saccade disconjugacy, subjects again performed the memory-guided saccade paradigm under monocular viewing (the eye wearing the magnifier was viewing).

Visually-guided saccades to non-disparate targets

This condition was run at the end of the experiment for a few of the subjects. It aimed to test for the transfer of learning from memory-guided saccades to visually-guided saccades. Viewing was monocular (with the eye wearing the magnifier), and saccades were elicited with the same standard saccade paradigm used for calibration (see above).

Data analysis

A linear function was used to fit the calibration data. Saccade onset was determined at the point where eye velocity reached 5% of the peak velocity; saccade offset was taken as the time when eye velocity dropped below 10°/s. When dynamic overshoot occurred (a small backward saccade that follows the main saccade with zero latency; see Kapoula et al. 1986), saccade offset was taken at the endpoint of dynamic overshoot. Examples of saccades with dynamic overshoot are shown in Fig. 1; dynamic overshoot is more clearly seen in the abducting eye (left eye in Fig. 1A, right eye in Fig. 1B). Post-saccadic eye drift was determined for a period of 160 ms after saccade offset or dynamic overshoot, if present. This value was chosen to be close to that required to reach the steady-state position in lesioned animals that develop ocular drift (e.g., Optican and Robinson 1980). More recent studies, however, (e.g., Inchingolo et al. 1996), have shown the presence of longer time-constant or post-saccadic drift with multiple components. Consequently, we also measured the amplitude of the drift and its disconjugacy over longer period of about 600 ms.

The accuracy of the saccade relative to the location of the target was of secondary interest in this study; it was analyzed only for saccades during training, and these results will be briefly reported in the discussion. The results to be presented concentrate on the disconjugacy of the saccades (the difference between the two eyes). Abnormally slow saccades or saccades associated with blinks were discarded. For each individual saccade, we measured – in degrees – the left-right eye difference in the amplitude of the saccade and of the post-saccadic eye drift. We use the term "intrasaccadic disconjugacy" to denote the difference in amplitude of the saccades. Positive values indicate convergent disconjugacy: saccade amplitude is larger in the adducting eye or it has more onward drift than in the abducting eye (the right eye is abducting for rightward saccades, the left eye for leftward saccades). Statistics were performed using the Student's *t*-test.

The analysis was performed separately for centrifugal and centripetal saccades. Recall that the centripetal saccades were triggered by the onset of the central dot, indicating the beginning of the next trial. These saccades were, therefore, visually-guided. The results to be presented next are the centrifugal saccades, which were memory-guided.

Results

Figure 1A shows typical binocular recordings of leftward memory-guided saccades. Note that all saccades of the left abducting eye showed dynamic overshoot of similar amplitude. Dynamic overshoot occurred for 36%, 61%, and 37% of the leftward saccades of the left eye before, during, and after training, respectively. As in prior studies (e.g., Kapoula et al. 1990), saccade end was taken at the end of dynamic overshoot. The saccade to non-disparate target recorded before training showed divergent disconjugacy. The eyes diverged at the beginning of the saccade and converged later by a smaller amount; the net change over the saccade (taken at the end of dynamic overshoot) was still divergent. In contrast, the saccade after about 2 min of training, i.e., after only 30 trials, showed substantial convergent disconjugacy, as required by the disparity of the target. The initial divergence was still present, but smaller, and was rapidly reversed to convergent disconjugacy; the net change over the saccade (also taken at the end of dynamic overshoot) was convergent. The saccade recorded after about 15 min of training, i.e., 225 trials, showed a net convergent disconjugacy only slightly larger than that shown at time 2 min. This disconjugacy was based on the ability to memorize disparity information for 1 s or to retain the motor command for a disconjugate saccade for 1 s. Interestingly, the saccade to a non-disparate target recorded after the 15 min of training retained a large convergent disconjugacy, even though there was no disparity in the preceding 3–5 min (interval from the end of training). This indicates an ability to memorize disparity even longer, i.e., for a few minutes. It should be noted that the disconjugate drift in the first 200 ms after the saccade or its dynamic overshoot was also convergent, but considerably smaller in amplitude than the net disconjugacy over the saccade; the direction of drift later reversed once or twice (Fig. 1A t=2 min, t=15 min). Figure 1B shows rightward memory-guided saccades. Note again the presence of dynamic overshoot, particularly for the right abducting eye. The frequency of dynamic overshoot for the right eye was 79%, 65%, and 67% before, during, and after training, respectively. The saccade before training had small divergent disconjugacy (net change at the end of dynamic overshoot). The saccades during training, particularly that after 15 min of training, showed increased divergent disconjugacy, as required by the disparity of the remembered target. The saccade to non-disparate targets recorded after training retained increased divergent disconjugacy. Note that training produced divergent disconjugacy regardless of the dynamic overshoot by increasing the initial divergent component. Disconjugate post-saccadic drift was small.

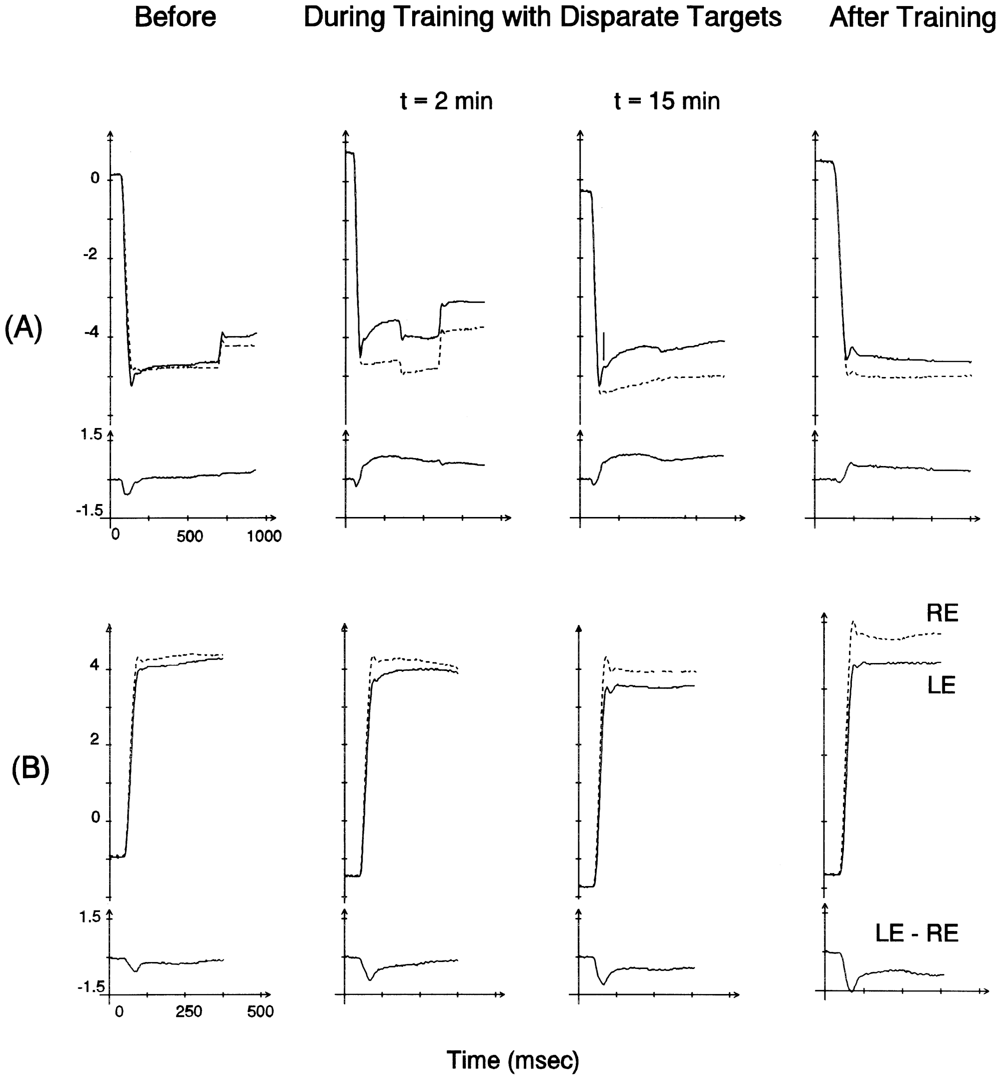

Fig. 1 Typical binocular recordings of leftward (**A**) and rightward (**B**) memory-guided saccades from subject ZK. The *solid line* is the position trace of the left eye in degrees (*LE*), the *dotted line* is that of the right eye (*RE*). The *lower trace* is the disconjugacy trace (the difference between the left and the right eye). Divergent disconjugacy is negative, convergent disconjugacy is positive. *Vertical tic* on the trace of the left eye, recording t=15 min, indicates the end of dynamic overshoot. Before and after training, the subject viewed monocularly with the right eye. During training, the subject viewed binocularly with the 8% magnifier in front of the right eye. Thus, the memorized target was disparate in the two eyes; the disparity was convergent for leftward positions, divergent for rightward positions

Figure 2 shows the time course of learning of disconjugacy for three of the subjects (solid lines). The time course was variable, but short for all three subjects. It took approximately 2 min, 6 min, and 8 min for subjects ZK, ST, and FL, respectively, to learn to make disconjugate saccades, as required by the disparity of the remembered target. The value of disconjugacy reached significance somewhere between 1.6 and 6 min for subject ST, between 4 and 8 min for subject FL, and in the first 2 min for subject ZK (Student's *t*-test comparing the mean disconjugacy before training, indicated by the thick-line segment on the ordinate, and the mean disconjugacy at different time points of training). Note that the increase of disconjugacy with time was not continuous, particularly for the first two subjects. At the beginning of training, the amplitude of the disconjugacy was smaller than required (dotted line); it approached or exceeded the requirement (ZK) towards the end of training.

Figure 3 shows results from six subjects. For all subjects, baseline saccades (hatched bars) were disconjugate even though the remembered target did not contain disparity. This inherent disconjugacy was divergent for all subjects, regardless of the direction of the saccade. For visually-guided saccades (measured in the same session during the calibration task), the inherent disconjugacy was also divergent. Eight of the twelve means of disconjugacy of memory-guided saccades shown in Fig. 3 were larger than the corresponding means of the disconjugacy of visually-guided saccades to non-disparate targets. The group mean disconjugacy of visually-guided saccades to non-disparate targets was divergent (–0.24±0.81° standard deviation, n=12); this value is similar to that reported by earlier studies (<0.3° for saccades with amplitudes below 20°, see Collewijn et al. 1988). The group mean disconjugacy for memory-guided saccades was also divergent, but larger in amplitude (–0.64±0.41°, n=12). Thus, the degree of the binocular coordination of memory-guided saccades to non-disparate targets was poorer than that known for visually-guided saccades.

During training, the disparity of the remembered target required a disconjugacy that was proportional to the eccentricity of the target and, consequently, to the amplitude of the saccade. The same target eccentricities were used for all subjects, and the average requirement (indicated

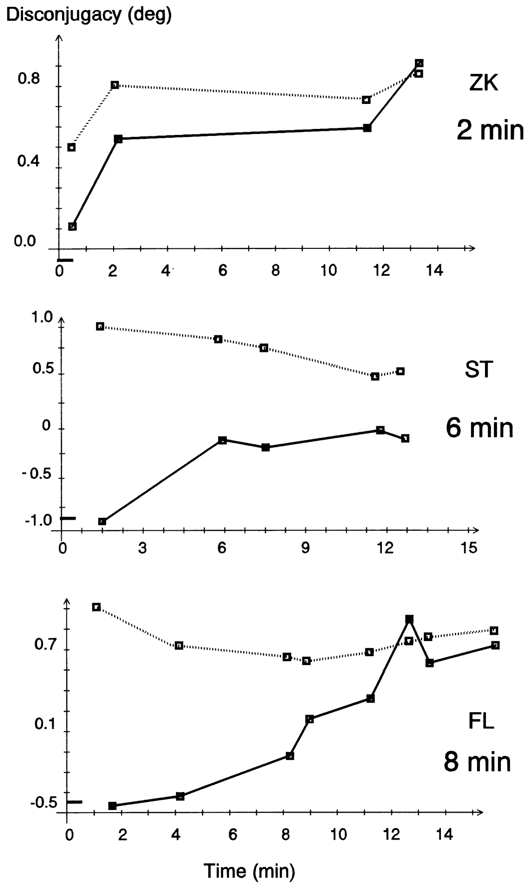

Fig. 2 Time course of learning. Solid lines indicate the disconjugacy of leftward saccades during training, *dotted lines* indicate the disconjugacy required by the disparity of the remembered target. Each *point* averages 12 saccades for subjects *ST* and *FL* and 24 saccades for subject *ZK*. *Thick line segments* on the y-axis indicate the average disconjugacy for memory-guided saccades to non-disparate targets recorded under monocular viewing before training. For all subjects, the remembered target was larger in the right eye, calling for convergent disconjugacy. Substantial convergent disconjugacy developed rapidly for all subjects

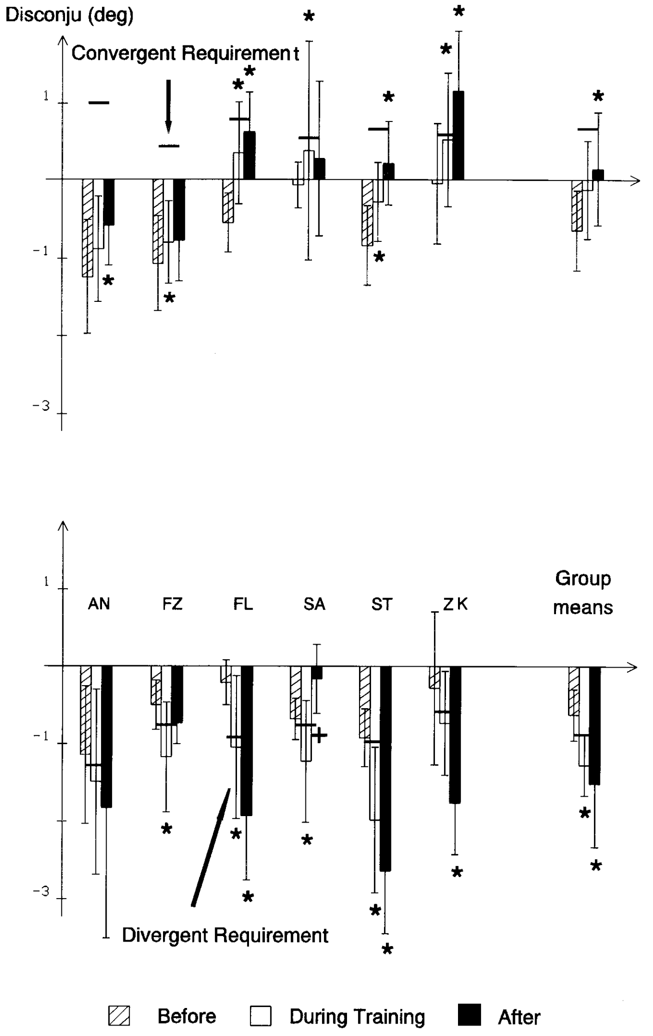

Fig. 3 Disconjugacy of memory-guided saccades before during and after training. *Bars* are individual means of disconjugacy together with standard deviations. *Horizontal lines* indicate the disconjugacy required by the magnifier during the training period. All subjects except ST wore the magnifier on the right eye; the requirement was convergent for leftward saccades, divergent for rightward saccades. Pre- and post-training means are based on 10–30 saccades; means during training are based on 50–150 saccades. Group means (n=6) before, during, and after training. *Asterisks* indicate a statistically significant change at the level $P<0.05$ (Student's t-test, comparison of the mean during training with the mean before training and the means before and after training). *Crosses* indicate a significant change in the opposite direction

by horizontal lines in Fig. 3) ranged from 0.6° to 0.9° for five of the six subjects; individual small differences in the average requirement were due to withdrawing of abnormally slow saccades and saccades associated with blinks. For each subject, the average amplitude of the saccades retained was very similar (within 1–2°) for the three testing conditions (before, during, and after training). Thus, the differences in the disconjugacy of the saccades between conditions to be reported below showed learning effects for similar sizes of saccades.

During training (empty bars), for all subjects, the intra-saccadic disconjugacy changed in the direction required by the disparity of the remembered target. When the remembered target required convergent disconjugacy, the inherent divergent disconjugacy (the net disconjugacy remaining at the offset of the saccade) decreased or reversed to convergent disconjugacy. The change was convergent in all cases; it was statistically significant (indicated by asterisks) for all subjects except AN. Memory-guided saccades to non-disparate targets, recorded subsequently in the monocular viewing condition (black bars), also showed convergent changes: the disconjugacy was significantly more convergent than the corresponding value of inherent disconjugacy for four of the six subjects. Thus, the learned disconjugacy was retained even though no disparity was sensed in the preceding 3–5 min.

When the remembered target required divergent disconjugacy during training, all subjects developed additional divergent disconjugacy. The change was statistically significant for all subjects except AN and ZK. Increased divergent disconjugacy was present for the after training control condition where the target was no longer disparate. Three of the six individual values of disconjugacy after training were significantly more divergent than the corresponding values of inherent disconjugacy.

Three of the four group means (convergent requirement after training, divergent requirement during and after training) were significantly different from the corresponding group mean of the inherent disconjugacy (before). The actual group means during and after training were larger for the divergent than for the convergent requirement, but the change from the before value was similar for the two requirements.

For either requirement, several individual mean values in the after-training condition were larger than those in the training condition. This was due to the fact that training values average disconjugacy over the total period of 15 min of training, including saccades at the beginning of training, for which the learning effect was weaker (see Fig. 2). Inspection of scatter plots of individual data showed that, for all subjects, values of disconjugacy after training were very similar to those at the end of the training period.

Was the actual disconjugacy perfectly adjusted to the requirement? For targets with convergent disparity, the average disconjugacy was convergent in three cases only; for all cases except one (Fig. 3, ZK after-training), the disconjugacy was below the requirement. In contrast, for targets with divergent disparity, all individual means averaging disconjugacy over the total period of 15 min were divergent and larger in amplitude than the requirement (indicated by horizontal lines, Fig. 3). The group mean ratio (disconjugacy/requirement, *n*=6 subjects) was as high as 1.52±0.35 and 1.74±0.97 for the during-training and after-training conditions, respectively. This excessive divergence most likely resulted from the addition of the learned disconjugacy to the inherent divergent disconjugacy. Similarly, the decreased values of convergence could be due to the substraction of the inherent divergent disconjugacy. The changes in the disconjugacy from the before-training values (pre-after-training differences) better reflected how the learned disconjugacy responded to the requirement. These changes were larger than those required for both types of disconjugacy. The group mean ratio (change in disconjugacy/requirement) was 1.19±0.56 and 1.23±0.72 for the convergent and divergent requirement, respectively. These observations suggest an overestimation of the disparity, i.e., of the position in 3D space of the remembered target.

The disparity due to the magnifier increased with the eccentricity of the target. Yet, a positive correlation between the amplitude of the disconjugacy and the amplitude of the saccades was observed only for saccades to remembered targets with divergent disparity; individual coefficients of correlation (*r*, Bravais-Pearson) ranged between 0.35 and 0.81 and were statistically significant for all subjects. In contrast, for saccades requiring convergent disconjugacy, significant positive correlation occurred only for subject SA (*r*=0.63). Thus, during training the disconjugacy of memory-guided saccades was not perfectly adjusted to the disparity of the target. Saccades to non-disparate targets recorded before and after training showed no correlation, even though saccades after training retained substantial divergent disconjugacy.

Post-saccadic drift and slow vergence

Disconjugacy in eye drift was examined over the first 160 ms after the saccade. Similar to visually guided saccades, the inherent post-saccadic eye drift of memory-guided saccades was predominately convergent regardless of the saccade direction, 0.17±0.34° and 0.03±0.42° (*n*=6 subjects) for the two saccade directions. Training with disparate remembered targets did not cause a significant change in these values. When the remembered target required a divergent movement, there was a tendency for post-saccadic drift to become more divergent (0.03±0.42°, –0.06±0.57°, –0.03±0.72°; group mean before, during, and after training, respectively); this, however, did not reach statistical significance.

Disconjugate drift, averaged over the longer period of 600 ms after the saccade, was also mostly convergent. Before training, the group mean amplitude of such drift was 0.35±0.19° and 0.06±0.27° (mean of six subjects±standard deviation) for leftward and rightward saccades, respectively. During training, statistically significant changes from the normal values in the appropriate direction occurred for only three of the twelve cases (the mean change was 0.21±0.08°, *n*=69 for subject ST convergent requirement; 0.14±0.04°, *n*=219 for subject FZ, divergent; and –0.24±0.09°, *n*=67 for subject SA, divergent). After training, there were only two instances of significant appropriate change (0.63±0.24°, *n*=41 for subject AN, convergent requirement; –0.24±0.09° for SA, divergent). Three of the five changes in post-saccadic drift were much smaller (2–5 times less) than the change in the disconjugacy of the amplitude of the saccade. For instance, for subject FZ with rightward saccades, the pre-training change in the disconjugacy of the amplitude of saccades was 0.7° (see Fig. 3), while the change in the post-saccadic drift was only 0.14°. Thus, the change occurring during the 30–100 ms for which the saccade lasts was five times larger than the change during the post-saccadic period of about 600 ms. In six other cases, disconjugacy of post-saccadic eye drift changed significantly, but in the wrong direction (the changes were convergent where they should be divergent and vice versa). In the remaining cases, no significant change occurred. The group mean values remained unchanged for both saccade directions and for both conditions, during and after training. Since the contribution of a slow vergence movement over a period of 600 ms was small or absent, its contribution during the brief duration of the saccade (30–100 ms) was negligible. These observations are in agreement with prior studies (e.g., Kapoula et al. 1995) and show that the learned disconjugacy mainly altered the amplitude of the saccade. It did so by means of a fast, saccade-related mechanism rather than by the superposition of a slow vergence movement starting with the saccade and following afterwards.

In summary, this study shows that normal subjects can rapidly learn to make disconjugate saccades even to remembered disparate targets. Learning occurs even for saccades in the dark and in the absence of visual feedback after the saccade.

Experiment 2

To further explore the capacity of target disparity to alter the conjugacy of memory-guided saccades, we ran a second experiment, in which the delay of memory in each training trial was prolonged to 2 s. All other aspects of the experimental procedure were the same as those of the first experiment described in Materials and methods. Five normal subjects were trained for 15 min with the magnifier in front of their right eye; three of the subjects had participated in the first experiment (FZ, FL, and ZK). The results of the second experiment are shown in Fig. 4. Significant changes in the appropriate direction occurred only for subject ZK with divergent requirement and for subject FZ with convergent requirement. In the remaining cases, the changes were either in the wrong direction (FL and VE) or not significant. The group means showed no significant change from the values of the inherent disconjugacy, neither for the training nor for the after-training condition. Thus, the short-term (1 s) and, consequently, the longer-term (3–5 min) learning failed when the memory delay was prolonged to 2 s.

Additional observations

Centrifugal visually guided saccades

For the first experiment, we also compared the disconjugacy of centrifugal visually guided saccades to non-disparate targets recorded before and after training. For all four subjects examined (AN, FL, FZ, ZK), rightward centrifugal visually guided saccades to non-disparate targets acquired a divergent disconjugacy similar to memory-guided saccades to disparate targets. The average change from the disconjugacy of visually guided centrifugal saccades recorded before training was 1.11±0.44° (*n*=23), 1.13±0.27° (*n*=46), 1.45±0.20° (*n*=34), and 0.65±0.23° (*n*=27) for subjects AN, FZ, FL, and ZK, respectively; all these changes were statistically significant. It should be emphasized that centrifugal visually guided saccades were recorded under monocular viewing and were never associated with disparity. Thus, disconjugate learning was present even for the non-trained visually guided saccades.

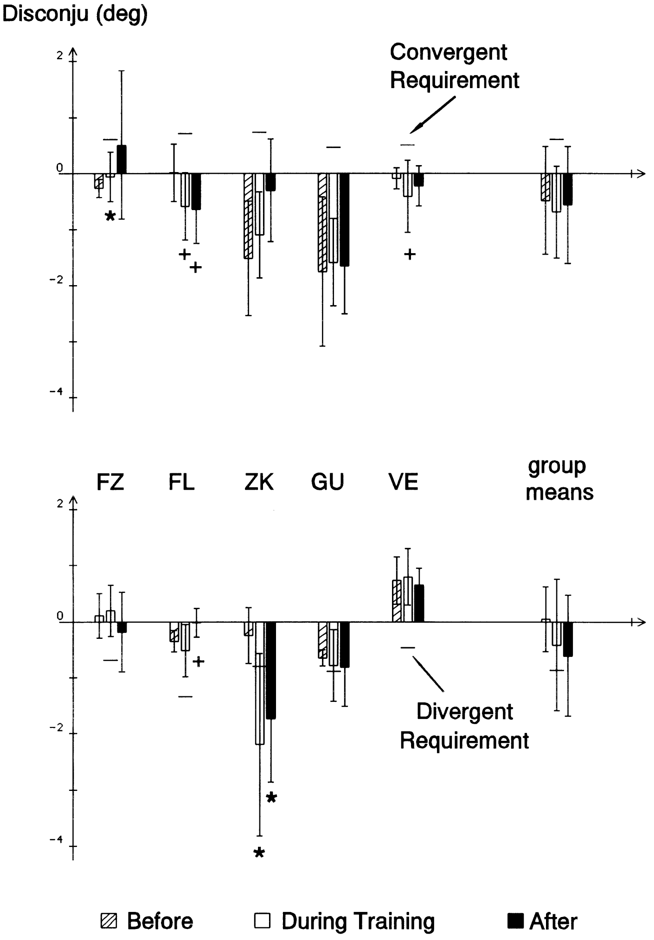

Fig. 4 Individual means of the disconjugacy of memory-guided saccades and their standard deviations. Before and after-training means are based on 10–24 saccades; means during training are based on 37–116 saccades. The memory delay was 2 s for all conditions (before, during, and after training). *Horizontal lines* indicate the disconjugacy required by the disparity of the target due to the magnifier. Group means are based on the number of subjects (five). Other notations as in Fig. 3

Discussion

Inherent disconjugacy of memory-guided saccades

Israël (1992) and Israël et al. (1993) described the accuracy characteristics of visual memory-guided saccades and the effect of a memory delay. These studies, however, used bitemporal EOG recordings of eye movements and did not provide any information about the binocular control of memory-guided saccades. Our study describes, for the first time, the degree of binocular coordination of memory-guided saccades. Similar to visually guided saccades, memory-guided saccades show transient divergent disconjugacy followed by convergent post-saccadic drift. The amplitude of the disconjugacy is subject-dependent and could be larger than that for visually guided saccades. This stereotyped pattern of divergent disconjugacy has been attributed to peripheral causes, such as differences in the mechanical properties of the lateral and medial rectus or differences in the delay of arrival of premotor signals at the motoneurons (e.g., Zee et al. 1992). That memory-guided saccades show the same pattern of disconjugacy is consistent with such peripheral explanations.

Learning to make disconjugate memory-guided saccades

Our main interest in this study was to probe the capacity for modifying the inherent disconjugacy of memory-guided saccades. We show, for the first time, that the inherent disconjugacy can be rapidly modified by the disparity of remembered targets flashed 1 s earlier. Such modification occurs after only 2–8 min; that is, after only 30–120 trials. This time course, albeit subject-dependent, is remarkably short. It is as short as that reported for visually guided saccades by Kapoula et al. (1995) and by Van der Steen and Bruno (1995). Furthermore, we show an ability to retain the learned disconjugacy for several minutes in the absence of any disparity information. This indicates learning based on longer-term memory. Importantly, memorized disparity mainly altered the amplitude of the saccade. Changes in post-saccadic eye drift were considerably smaller and idiosyncratic. Thus, similar to visual disparity, memorized disparity stimulates a saccade-related learning mechanism; a slow vergence movement superimposed on the saccade cannot be excluded, but its contribution was not significant. The disconjugacy during the saccade could be produced either by the saccadic system or by a fast vergence system coupled to the saccade, as suggested by Zee et al. (1992). This is an important point, but cannot be answered by behavioral studies.

Another point that should be addressed before discussing further memory-based motor learning is the duration of target presentation. One could argue that, in the first training trials, the acquisition of the target was poor due to its brief presentation (100 ms). With repetition, target acquisition improved, thereby allowing saccades to be produced with appropriate disconjugacy. In other words, the training effect shown in Fig. 2 manifests amelioration of target acquisition and not motor learning. That this is not the case has been shown by additional experiments run on two subjects (ZK and MB), during which the target to be remembered in each training trial was presented for 1000 ms and 500 ms, respectively. The findings are very similar to those presented in the Results section. For instance, when the remembered target required convergent disconjugacy, saccades developed convergent disconjugacy. The average change was 0.86±0.26° for subject ZK (n=62) and 0.46±0.15° (n=138) for subject MB. Convergent disconjugacy was correlated with the amplitude of the saccade for subject ZK (r=0.68), but not for subject MB. The change in disconjugacy reached statistical significance (relative to the value before training) somewhere between 7 and 10 min for subject ZK and somewhere between 2 and 5 min for subject MP. This time course is comparable or even slower (subject ZK) than those presented in Fig. 2. Thus, saccade disconjugacy develops only after repeated trials, even when the time available for target acquisition is long. Consequently, the modification of the disconjugacy of saccades with repetition manifests learning. A subsequent study (Kapoula et al. 1997) showed that learning fails when saccades are not made and provides further support for motor learning. In that study, a training period of 15 min was applied using a paradigm very similar to that presented here. The only difference was that for each training trial, after the 1-s memory delay, the subject had to maintain fixation at center. Such sensory or static training did not produce any lasting change in the disconjugacy of memory-guided saccades to non-disparate targets recorded afterwards. Thus, disparity memorization and learning have a motor basis.

Adaptation versus map learning

Prior studies (Kapoula et al. 1995; Van der Steen and Bruno 1995) have also shown retention of the learned saccade disconjugacy in neutral conditions (e.g., under monocular viewing). This was considered to be evidence for an adaptive parametric modification of the saccadic system by Van der Steen and Bruno (1995). In the above studies, the disparate targets were continuously present during training. Subjects could use immediate peripheral disparity cues to program every saccade; after the saccade, they could use residual disparity as an error signal on their motor performance. A slow iterative process of reducing this error could indeed be involved and lead to an adaptive parametric readjustment of the saccade signals. This is one way of thinking about oculomotor learning or adaptation. Consistent detection of a visual error at the end of the saccade is interpreted by the CNS as motor misperformance, calling for a parametric readjustment of the saccade neural signals. In the present study, there was no post-saccadic visual feedback to drive adaptation or readjustment of the saccadic system. Disparity information was briefly available in the periphery for only 100 ms. Yet learning occurred. Thus, this study provides, for the first time, evidence for another, high-level learning mechanism based on memory; this mechanism is also capable of rapidly altering saccade conjugacy. We propose a map learning mechanism rather than adaptation aimed at reducing an error. We suggest that, with training, subjects learn to localize better the target to remember in 3D space. On the basis of the disparity sensed briefly over successive trials at the left versus right visual periphery, but also on internal loops or proprioceptive feedback related to the disconjugate movements already performed (motor basis), the brain reconstructs a 3D representation of the surface of the targets. Namely, the arc upon which the targets are presented would be represented as tilted in space by the amount corresponding to the distribution of disparity. It is thus possible to direct gaze in 3D space even when a target presented on this surface is no longer disparate.

Time course of learning, correlation, role of transient disconjugacy

As in our prior studies (Kapoula et al. 1995; Eggert and Kapoula 1995), the disconjugacy developed after a short training period, but did not always increase smoothly with time; it was also not always positively correlated with the amplitude of the saccade, as required by the disparity. A positive correlation was found only during training and only when the required disconjugacy was divergent. This correlation might have been facilitated by the inherent divergent disconjugacy present even for saccades to non-disparate targets. Indeed, Collewijn et al. (1995) reported that the first divergent component of the intrasaccadic disconjugacy increases with saccade amplitude, at least for saccades below 40° in size.

Could the inherent transient disconjugacy facilitate disconjugate learning? In our study, the learned disconjugacy seemed to be superimposed on the transient inherent disconjugacy. Examples of these are shown in Fig. 1A during training: a small divergence occurs at the onset of the saccade even when convergence is required. Our observations are consistent with studies of combined saccade-vergence movements to targets located in real 3D space. Indeed, Collewijn et al. (1995) and Maxwell and King (1992) reported in humans and in monkeys, respectively, intrusion of divergence even when the saccade is combined with convergence. Collewijn et al. (1995) discussed the possibility of a central origin of the transient inherent disconjugacy during the saccades, which would serve to build additional divergence or convergence such as required, for instance, for fixating targets in real 3D space that differ both in direction and in distance. Bruno et al. (1995) also considered a role of the transient vergence in disconjugate adaptation. In the present study, disconjugacy was correlated with the amplitude of the saccade only during training and only for divergent requirement. Also, the learned divergent disconjugacy was present even for visually guided centrifugal saccades (see below). These aspects of the results suggest some facilitation for making saccades with divergent disconjugacy. However, further investigation of saccade dynamics and trajectory is needed to test if and how the intrinsic divergent disconjugacy facilitates disconjugate learning.

Whatever the role of the transient inherent disconjugacy is, if the learned disconjugacy was mediated by a parametric adjustment, one would expect a strong and persisting correlation between disconjugacy and saccade size, regardless of the direction of the saccade. Our findings did not show such behavior. The absence of strong persisting correlation and the irregular time course of learning are more compatible with the idea of associative memory-based learning rather than a low-level oculomotor parametric readjustment.

After training, the learned disconjugacy was present even in visually guided centrifugal saccades. However, whether learning was specific to memory-guided saccades is not known. Deubel (1995) reported evidence for the existence of distinct adaptive mechanisms for modifying the gain of reactive versus more volitional saccadic eye movements. Further investigation is needed to test differentially the possibility of disconjugate learning for memory versus visually guided saccades.

Overshooting of memory-guided saccades

Memory-guided saccades to non-disparate targets tend to overshoot their target (see Israël 1992). Consistently with this study, we observed a tendency for overshooting in three of the six subjects. The mean gain (amplitude of the primary saccade averaged over the two eyes/target position) was 1.11±1.48 (*n*=106), 1.09±1.33 (*n*=129), and 1.12±0.25 (*n*=66) for subjects AN, SA, and ZK, respectively. Subjects AN and SA overshot all target positions, while subject ZK overshot only the smallest eccentricities (5°). The other subjects undershot most target positions (the gain was 0.88, 0.99, 0.95 for subjects FZ, FL, and ST, respectively). The group mean gain was close to 1 and this contrasts the undershooting of visually guided saccades (e.g., Collewijn et al. 1988). Similarly, the change in the disconjugacy in the present study was larger than required (pre-after-training differences). Thus, overshooting could be a common property of all memory-guided saccades.

Functional and theoretical considerations

Why would the CNS care to modify the disconjugacy of the saccades in the dark, since there was no visual feedback after the saccade and no error to correct? Most likely, the saccadic system is sensitive to disparity and cannot ignore it even when there is no visual penalty after the saccade. This sensitivity might be due to the permanent association of saccades and disparity we experience continuously during exploration of the natural 3D visual world. The disparity induced by the afocal magnifier mimics such natural situations of targets differing in both direction and depth. As already pointed out, our situation is a reduced-cue situation, where the only cue to depth is disparity without the contribution of accommodation or other high-level depth cues. Yet, saccades become rapidly disconjugate as long as one of the conditioning stimuli, e.g., disparity, is present. The most remarkable new finding is that saccades acquire disconjugacy even when the conditioning stimulus (disparity) is memorized. Such behavior implies the existence of a saccade-targeting system in three-dimensional space gifted with three-dimensional memory and learning capacity. Using a different experimental approach, Chaturverdi and Gisbergen (1997) recently demonstrated that saccadic gain adaptation can be specific to the depth-component of the stimulus. They came to a conclusion similar to ours, i.e., the need to include the depth dimension in the study and modelling of the saccadic system. The present study shows, for the first time, 3D memory control of saccades. Our ability to obtain rapidly bifoveal fixation of targets located at different depths in complex 3D environment could be partially based on such 3D memory control. In patients, memory control of the binocular coordination of saccades could help to attenuate visual and motor deficits resulting from unilateral oculomotor pathologies. When exploring real targets in complex 3D environment, the disconjugacy required from one saccade to another can be highly variable and not correlated with the amplitude of the saccade (as is the case for most experimental situations). Memory of the disparity of targets of particular interest, i.e., pre-knowledge of the location of such targets in a 3D representation of space, could help in rapidly obtaining single binocular vision for both normals and patients. The memory-based mechanism uncovered in the simplified experimental situations used here is complementary to vision and is most likely used by the brain for a more efficient control of gaze shifts in natural 3D space.

Three-dimensional memory, however, seems to be fragile. For memory-guided saccades to non-disparate targets, increasing the memory delay from 2 to 12 s only has a mild effect on their accuracy (Israel 1992). In contrast, our second experiment shows that target disparity fails to induce saccade disconjugacy if the memory delay is 2 s. Memory of disparity information could decay rapidly with time. Alternatively, it is not decay time per se that is important, but the execution of a saccade in a certain time interval after disparity coding. Disparity could be used for saccade programming only when a saccade is going to be executed shortly afterwards. The duration of target in 3D space presentation in the ability to memorize target position for longer than 1 s is another temporal aspect that deserves further investigation.

Substrate for disconjugate memory-guided saccades

The generation and execution of memory-guided saccades to non-disparate targets involve a complex cortical-basal ganglia-collicular circuit (Hikosaka and Wurtz 1989). The substrate for disconjugate memory-guided saccades to disparate targets is not known. How is disparity information memorized? One possibility would be the retention of sensory signals in the visual cortex coding disparity. Alternatively, the briefly sensed disparity error in the periphery leads to a disconjugacy motor command, which is retained during memory delay and executed together with the saccade. In other words, a sensorimotor transformation occurs and disparity information is memorized in motor coordinates. In monkey area LIP, cells discharge during the memory delay and during a saccade to a remembered target (Andersen et al. 1996). These neurons are also sensitive to depth and disparity and discharge before and during combined movements of saccades and vergence (Gnadt and Mays 1995). Thus, premotor signals necessary to make memory-guided disconjugate saccades to disparate targets could be provided by the parietal cortex.

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