Properties of Saccades in Duane Retraction Syndrome

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PURPOSE. To improve understanding of the binocular control of saccades by making high-resolution eye movement recordings in patients with unilateral Duane retraction syndrome (DRS) type I (marked by congenital absence of the sixth cranial nerve).

METHODS. Binocular eye movements were recorded in four patients in binocular viewing conditions during a saccade task.

RESULTS. *Affected-side gaze* showed normal saccades of the sound eye and undershooting saccades of the affected eye—evidence of intact interneurons, but deficient motoneurons, in the sixth-nerve nucleus on the affected side. Postsaccadic smooth onward drift followed undershooting saccades of the affected eye. *Sound-side gaze*, in the *centripetal* direction, showed relatively accurate saccades despite large offsets in initial position between the two eyes. In the *centrifugal* direction, there was a consistent undershoot of the affected eye. The sound eye showed unexpected overshoot. Postsaccadic drifts in opposite directions in the two eyes brought both eyes onto the target in an optimal time course.

CONCLUSIONS. Studying the characteristics of the saccadic system in this oculomotor disorder gives new insight into binocular control of saccades and adaptation. In these patients, the oculomotor system was not capable of adapting the pulse command to the two eyes separately, even though DRS offers clear advantages of independent control. In contrast, independent adaptation of the saccadic step command was sent to the two eyes. This supports the idea that the rapid part of the saccadic command is common to both eyes. (*Invest Ophthalmol Vis Sci.* 2005;46:3144–3151) DOI:10.1167/iovs.05-0060

Duane retraction syndrome (DRS) is an unusual congenital form of strabismus that occurs in approximately 1 in 50 patients with strabismus.[1–3] It causes horizontal eye movement limitations, as do other disorders, but it is unique in causing retraction of the globe, with palpebral fissure narrowing, on attempted adduction. All DRS patterns are caused by anomalous innervation of the lateral rectus muscle, in various degrees of severity (from no to almost normal innervation), and by secondary muscle changes (e.g., atrophy and fibrosis that re-

duces muscle elasticity). Three types of DRS are recognized, depending on the amount of aberrant innervation present, causing defective abduction (type I), defective adduction (type II), or both defective abduction and adduction (type III), based on clinical examination.[4]

The etiology of DRS has been very speculative. Early studies evoked structural abnormalities, such as posterior insertion of the medial rectus or an inelastic lateral rectus muscle. Electromyographic investigations found evidence of anomalous innervation of the lateral rectus of the affected eye. This paradoxical innervation (electrical activity during adduction, but not during abduction) is due to the misdirection of third nerve (IIIn) axons (normally destined for the medial rectus) to the lateral rectus.[5–7] Anatomic and histologic pathology show that during 4 to 8 weeks of gestation, there is maldevelopment (absent or partial development) or injury to developing structures of the sixth nerve (VIn) nucleus and nerve(s). Branches from the third nerve are then redirected to the lateral rectus muscle, causing a wide spectrum of anomalous innervations.[8] Affected subjects are rarely available for autopsy, because DRS is a benign disorder. However, absent sixth nerves and sixth nerve nuclei were reported in a bilateral DRS type III case,[9] and in a unilateral case with an absent sixth nerve on the affected side.[10] In the latter case, the abducens nucleus contained no motor neuron cell bodies, but did contain several small cell bodies, presumably the interneurons from VIn to IIIn. This was thought to explain the preservation of conjugate eye movements through the medial longitudinal fasciculus, even though the sixth nerve nucleus was absent. Recently, magnetic resonance imaging (MRI) has revealed aplasia of the sixth nerve, at its emergence from the inferior pons.[11,12] MRI has also been used to investigate up- and downshoot phenomena in adduction, where it showed minimal vertical displacement of the lateral rectus muscle in relation to the orbit.[13]

Eye movement recording is another noninvasive technique that has given valuable information about the central control of movement.[14–17] Unfortunately, many previous studies of DRS have provided only qualitative descriptions of eye movements. Previous studies involved a mix of all types of patients with DRS (types I, II, and III). Furthermore, the properties of saccades were analyzed without making any distinction between centrifugal and centripetal movements, thus ignoring the manifest asymmetry in DRS. All studies used low resolution techniques, such as electro-oculography.[18–21] Moore et al.[22] were the first to perform high-resolution recordings in two patients with DRS type I. In general, their findings supported the hypothesis that DRS results from a central reorganization of the ocular motor function in the brain stem. However, they reported no differences between the dynamic characteristics of adducting saccades in the affected eye and those of adducting or abducting saccades in the sound eye, which contradicted all previous reports. This unusual finding is probably due to the pooling of centrifugal and centripetal movements in their data analysis.

In this study, we conducted a more systematic investigation of DRS. First, the criteria of selection of the patients included in the study were very strict. Only unilateral DRS type I was studied; thus, all patients had an oculomotor disorder in which the abnormality in innervation was well defined and the aberrant innervation was less pronounced. We used high-resolution

FIGURE 1. Horizontal ocular motility of all subjects with unilateral DRS type I. Gaze to the right corresponds to sound-side gaze (SSG) and gaze to left corresponds to affected-side gaze (ASG) in subjects LT, JLB, and FDR, whose affected eye (AE) was the left one. It was the opposite in subject MB, whose right eye was affected. *Gaze to right*: mild limitation of adduction of the AE was noted in all subjects in SSG. Globe retraction and eyelid fissure narrowing was present in all to variable degrees. An upshooting of the AE occurred in attempted adduction in subject LT. *Primary position with head straight*: orthoposition of eyes in all subjects except for subject FDR, in whom a small 4° left eye esotropia was noted. *Gaze to left*: abduction deficit of the AE was severe in all subjects, but mostly in subject FDR, whose AE did not reach midline.
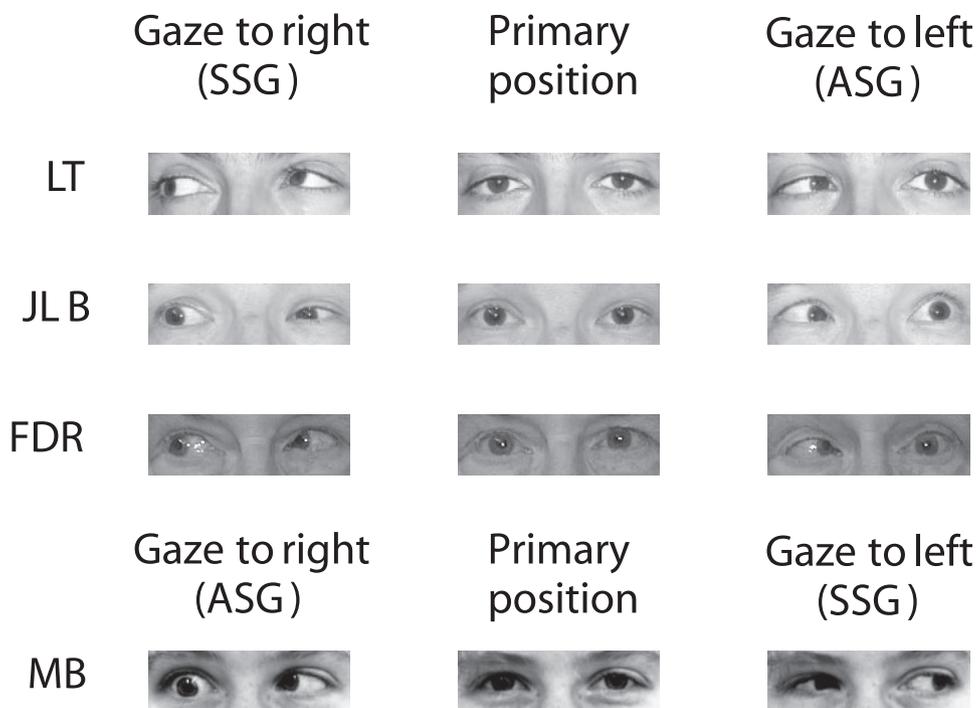
eye movement recording techniques so that saccade properties could be described qualitatively and quantitatively. Four different categories of saccades were analyzed separately: centrifugal and centripetal saccades for each side of gaze. Moreover, MRI verified the absence of the abducens nerve. The findings in the pathology of DRS type I allowed us to test two hypotheses about binocular control: The two eyes receive a common innervation during saccades (conjugate drive), or they receive independent (left eye and right eye) motor commands. We expect the adaptation of innervations to be different in the two cases.

METHODS

Clinical Examination of DRS Patterns

The patient inclusion criteria were based very strictly on clinical features. Only patients with classic, unilateral DRS (type I) without any ocular or systemic associated anomalies were included in the study. They had never had strabismus surgery. Four subjects were selected for study (LT, JLB, FDR, and MB). All had unilateral DRS of the left eye except subject MB whose right eye was affected. Horizontal ocular motility in each subject is shown in Figure 1. Snellen visual acuity was 6/6 at far and near for each eye with proper correction. Subjects FDR and MB wore myopic spectacle corrections. Only subject FDR had an abnormal head posture, with a 15° head turn to the left to keep binocular fusion because of affected-eye esotropia in primary position. The binocular vision was subnormal or normal in all subjects, but it had to be tested in the field of vision where the motility of the affected eye was complete. There was no anisometropia and no amblyopia. Anterior and posterior segment examination of the eyes showed no abnormalities.

Magnetic Resonance Imaging

Subject MB was scanned to investigate the abducens nerve at its emergence from the inferior pons and to observe the cross-sectional area of extraocular muscles (EOMs) in different directions of gaze (primary position, gaze to the right, and gaze to the left). All images were obtained on a 1.5-Tesla scanner (Intera NTscan; Philips Medical Systems, Best, The Netherlands) with a quadrature head coil.

High-resolution, fast spin-echo, T_2-weighted images of the brain stem showed the subarachnoid segment of the right and the left abducens nerves. Three-dimensional acquisition (in-plane resolution, 0.430×0.717 mm^2; slice thickness, 0.7 mm; and overlap, 0.35 mm) allowed the use of multiplanar reformatting to follow the nerve axis.

Fast spin-echo T_1-weighted images of the orbits were acquired in the coronal plane perpendicular to the orbital axis and in the axial direction along the axis of the optic nerve (in-plane resolution, 0.625×0.833 mm^2; slice thickness, 3 mm; and slice gap, 0.3 mm).

For each studied gaze position, we selected the axial images through the globe and the coronal images through the retrobulbar muscle cone, crossing the EOMs in their middle portion.

Experimental Setup

Subjects were seated in complete darkness with the head restrained by a chin-rest. They faced a 1-m distant tangent screen that spanned approximately 45° of the visual field. The visual target was a red laser spot back-projected onto a flat screen and moved horizontally under the control of a mirror-galvanometer. Recording of eye movements was performed with the scleral search coil technique (Skalar Medical BV, Delft, The Netherlands),[15,16] for subjects MB, LT, and FDR. One subject, JLB, was recorded with a high-frame-rate video tracking system (Chronos; Skalar Medical BV).[17] All the subjects gave informed consent. All procedures were approved by the Université Catholique de Louvain Ethics Committee, and the study protocol adhered to the guidelines set forth in the Declaration of Helsinki.

Paradigm

A *fixation-step-fixation* paradigm was used, in which a central fixation target (duration, 300–800 ms) was followed by a random step (size, −20° to +20°; and duration, 600–1600 ms) and a return back to central fixation. The goal was to generate centrifugal and centripetal saccades in the right and left directions. The positions of both eyes were recorded in binocular viewing conditions.

Data Acquisition and Analysis

Eye and target position were sampled at 500 Hz and stored on the hard disc of a computer for off-line analysis. Commercial software (MatLab; (MathWorks, Inc., Natick, MA) was used to implement digital filtering,

Subject MB

FIGURE 2. Axial-oblique reformatted T_2-weighted image of the brain stem at the pontomedullar level in subject MB. *Right arrow*: left sixth nerve at its emergence from the inferior pons in the subarachnoid space. *Left arrow*: clear absence of the *right* sixth nerve at the same level.

velocity, and acceleration estimation algorithms. Position signals were low-pass filtered by a zero-phase digital filter (autoregressive forward–backward filter; cutoff frequency, 50 Hz). Velocity and acceleration were derived from position signals by using a central difference algorithm. In our analysis, saccades were detected with an acceleration threshold of 750 deg/s^2.

Categorization of Saccades

For descriptive purposes, eye movements were divided into four categories, according to whether they were toward the *affected side* or the *sound side* and whether they were centripetal or centrifugal.

(Affected-side gaze was to the left in subjects LT, JLB, and FDR and to the right in subject MB.)

RESULTS

Magnetic Resonance Imaging

In axial–oblique reformatted images of the brain stem at the pontomedullary level in subject MB, we clearly saw the absence of the abducens nerve in the subarachnoid space on the right side (Fig. 2). The contraction and elongation of EOMs in primary position, affected-side gaze, and sound-side gaze in MB are shown on axial and coronal images of the orbits (Fig. 3). On coronal views through the middle portion of horizontal EOMs (Figs. 3D–F), line drawings were made to visualize the relative sizes of EOMs for each eye. For a movement to the sound side, the medial rectus (MR) of the affected eye and the lateral rectus (LR) of the sound eye must contract and the LR of the affected eye and the MR of the sound eye must elongate. It is the opposite for the affected-side gaze. In *primary position*, the eyes were aligned during constant fixation. There was no atrophy of the LR muscle body in the affected eye, despite the absence of innervation by the sixth nerve (Figs. 3B, 3E). In *affected-side gaze*, the sound eye's behavior was normal in adduction with contraction of the MR and elongation of the LR. There was an absence of abduction of the affected eye without a noticeable change in the muscle body cross-section of the LR and MR (Figs. 3A, 3D). In comparison, abduction of the fellow sound eye during sound-side gaze showed a fatter LR and a thinner MR (Figs. 3C, 3F). This represents normal muscle contraction and elongation during abduction of the eye. In *sound-side gaze*, the sound eye's behavior was normal, with contraction of the LR and elongation of the MR. The behavior of the affected eye was abnormal in adduction, with no elongation of the LR during contraction of the MR (Figs. 3C, 3F), indicating an abnormal co-contraction of MR and LR during adduction of the eye.
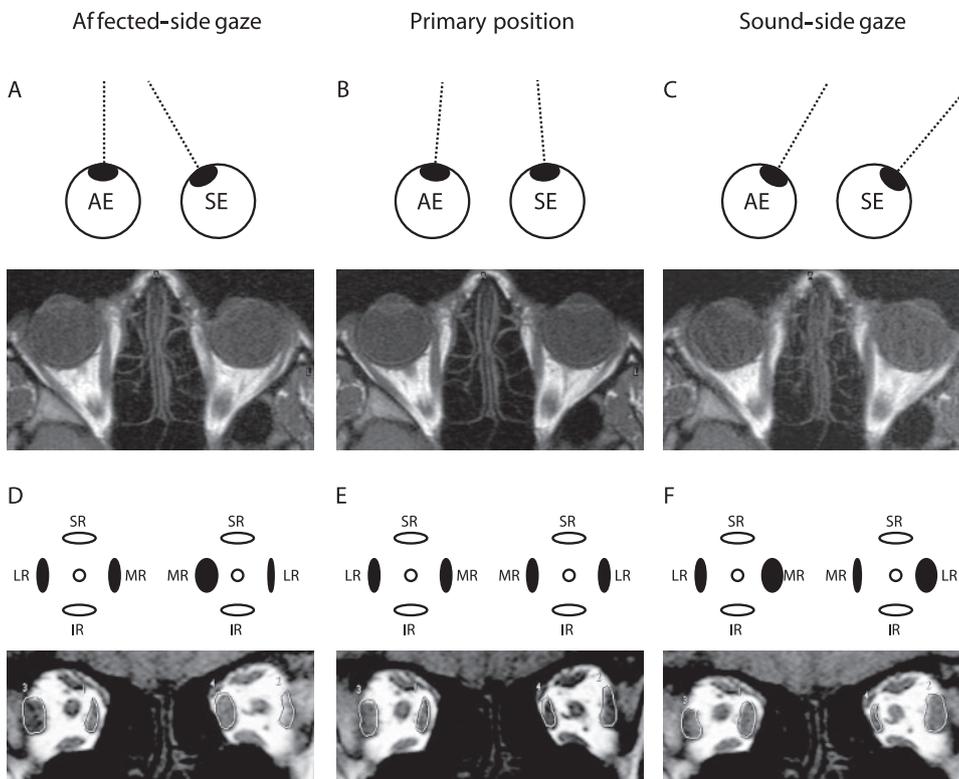

FIGURE 3. Axial (**A–C**) and coronal (**D–F**) T_1-weighted images through the orbits in subject MB, obtained during constant fixation to affected-side gaze (**A, D**), in primary position (**B, E**), and to sound-side gaze (**C, F**). The contour of the EOMs were manually drawn on coronal views through the middle portion of the EOMs to visualize the relative movements of the globes and the relative sizes of the EOMs in each eye in each direction of gaze. (1,2) The MR of the affected eye (AE) and LR of the sound eye (SE), respectively; (3, 4) the LR or the AE and the MR of the SE, respectively.
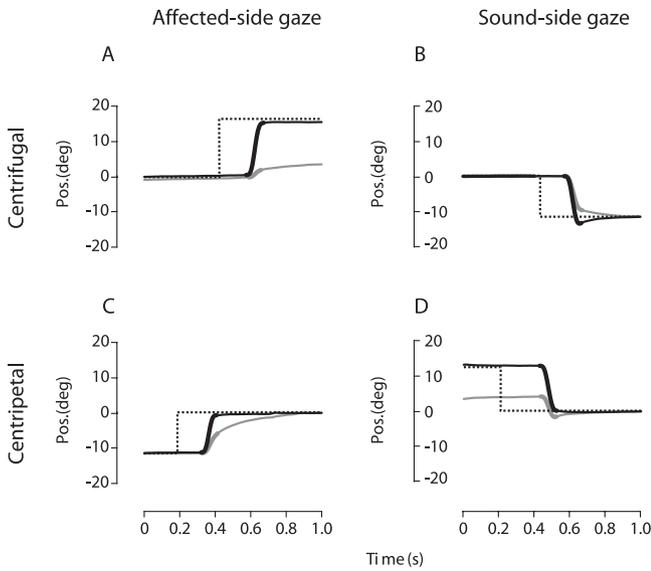
FIGURE 4. Traces of eye movements in subject MB: centrifugal to affected-side gaze (**A**), centrifugal to sound-side gaze (**B**), centripetal to affected-side gaze (**C**), and centripetal to sound-side gaze (**D**). *Black traces*: sound eye (LE); *gray traces*: affected right eye. Saccades are in *bold*.

Qualitative Analysis

Typical eye movements are shown for subject MB in Figure 4. Traces were subdivided into four categories: centrifugal to affected-side gaze (Fig. 4A), centrifugal to sound-side gaze (Fig. 4B), centripetal to affected-side gaze (Fig. 4C), and centripetal to sound-side gaze (Fig. 4D).

Each category of eye movement showed a fast saccadic phase, detected by the acceleration criterion and traced in bold. In some categories, there was a postsaccadic, smooth eye displacement (*postsaccadic drift*) correcting the interocular position error. The postsaccadic drift was either *onward* or *backward* relative to eye displacement. Abnormal saccades were detected by visually analyzing their velocity profile. Saccades were categorized as *normal* if there was a single peak, *double* when there were two positive peaks, *dynamic overshoot* when there was both a positive and a negative peak, and *abnormal* in all other cases.

Quantitative Analysis

Only normal saccades were included in the quantitative analysis. The relationship between saccade amplitudes of the affected and sound eyes for each category of eye movement in subject MB is shown in Figure 5. The relation was quite linear for all categories. In the *centrifugal direction to affected-side gaze* (Fig. 5A; see example Fig. 4A), saccades of the affected eye were very small in comparison with those of the sound eye (slope = 0.12). In the centripetal direction to affected-side gaze (Fig. 5C; see example Fig. 4C), saccade amplitude of the affected eye was larger than in the centrifugal direction but still less than in the sound eye (slope = 0.57). In the *centrifugal direction to sound-side gaze* (Fig. 5B; see example Fig. 4B), saccades in the affected eye showed their best performance compared with the sound eye (slope = 0.76). In the *centripetal direction to sound-side gaze* (Fig. 5D, see example Fig. 4D), the saccade of the affected eye was less than in the sound eye (slope = 0.29). Table 1 provides the statistics for each category of saccades and each subject. The slope of the linear regression is in bold. Despite the low gain of saccade amplitude of the affected eye compared with the sound eye, fusion was still obtained, with both eyes reaching the target (except centrifugal to affected-side gaze movements). It happens through postsaccadic smooth drift of one or both eyes, correcting the interocular position error. The amplitude of postsaccadic smooth drift for each eye of all subjects and for each
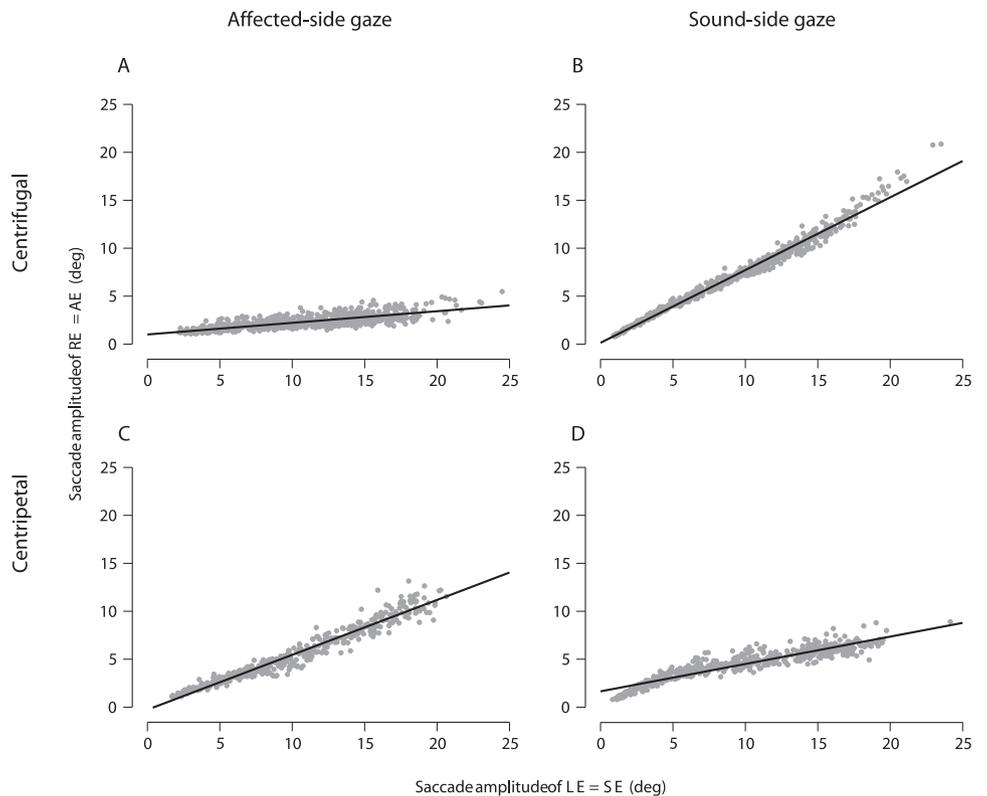

FIGURE 5. Linear relationship between saccade amplitude of affected and sound eyes in subject MB. Panel labels are as in Figure 4. The slope of the linear fit gives the saccadic gain (see Table 1).

TABLE 1. Correlation between Saccade Amplitude of Sound Eye and Affected Eye in Each Subject

	Affected-Side Gaze				Sound-Side Gaze			
	n	*r*	*P*	Equation	*n*	*r*	*P*	Equation
Centrifugal								
MB	672	0.76	0.00	$y = 1.01 + 0.12x$	605	0.99	0.00	$y = 0.13 + 0.76x$
LT	18	0.87	0.00	$y = 0.83 + 0.12x$	446	0.94	0.00	$y = 0.75 + 0.68x$
JLB	70	0.81	0.00	$y = 1.37 + 0.17x$	259	0.99	0.00	$y = 0.26 + 0.83x$
FDR	83	0.83	0.00	$y = 0.20 + 0.13x$	605	0.98	0.00	$y = 0.14 + 0.53x$
Centripetal								
MB	435	0.97	0.00	$y = 0.27 + 0.57x$	568	0.93	0.00	$y = 1.68 + 0.29x$
LT	151	0.94	0.00	$y = 0.29 + 0.49x$	304	0.89	0.00	$y = 0.96 + 0.30x$
JLB	193	0.98	0.00	$y = 0.68 + 0.66x$	201	0.94	0.00	$y = 1.53 + 0.43x$
FDR	322	0.95	0.00	$y = 0.67 + 0.51x$	80	0.95	0.00	$y = 0.88 + 0.24x$

category of eye movements is plotted in Figure 6. In *centrifugal to affected-side gaze movements* (Fig. 6A; see example Fig. 4A), there was no drift of the sound eye because the saccade was accurate. The affected eye showed a small drift, except for subject FDR. Drift was not noticeable in subject FDR, probably because the affected eye was more restricted in abduction and did not even reach the midline. For this category of eye movements, even after a postsaccadic drift, the affected eye could

not reach the target and there was an important residual interocular error. In *centripetal to affected-side gaze movements* (Fig. 6C; see example Fig. 4C), there was no drift of the sound eye because the saccade was accurate. The affected eye showed a drift in all subjects that drove the affected eye onto the target, reaching the same position as the sound eye. In *centrifugal to sound-side gaze* (Fig. 6B; see example Fig. 4B), all subjects showed an onward drift of the affected eye except

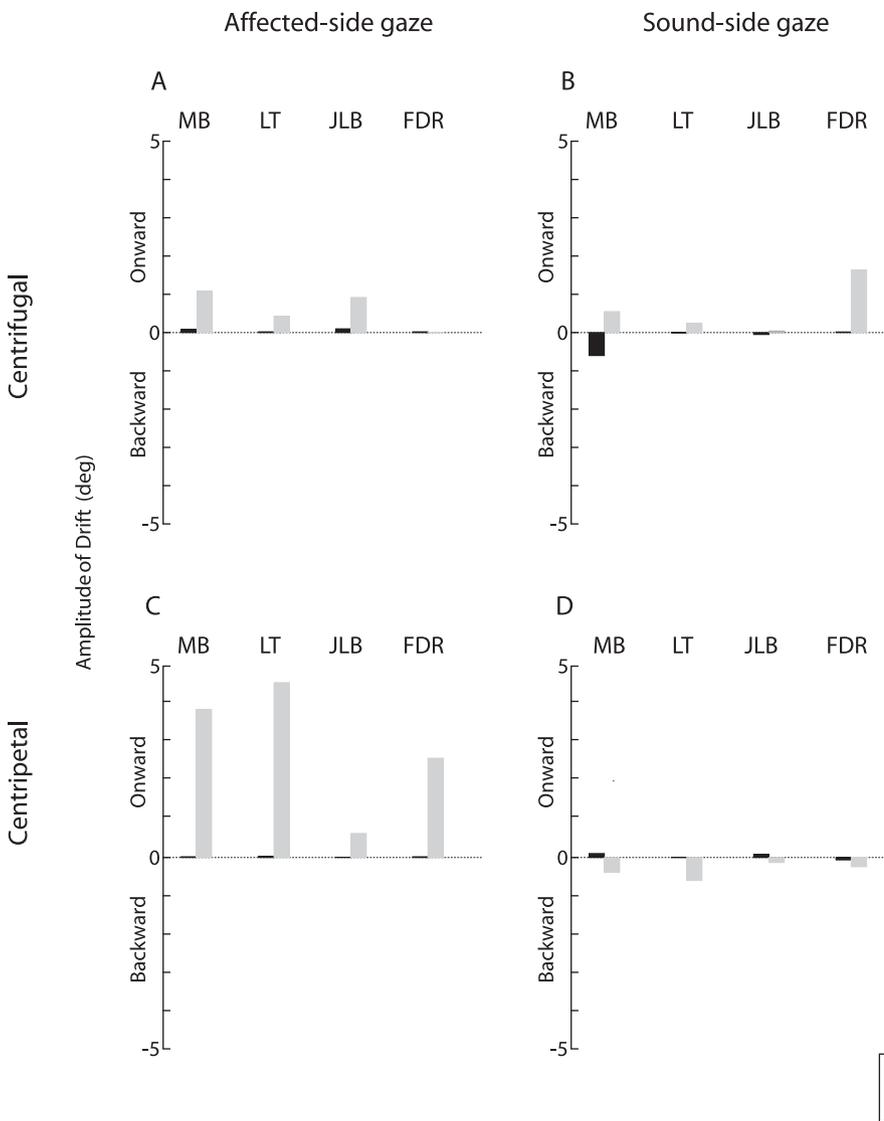**FIGURE 6.** Amplitude of smooth postsaccadic drift of each subject is plotted for centrifugal to affected-side (**A**) and sound-side gaze (**B**), and centripetal to affected-size gaze (**C**) and sound-side gaze (**D**). (■) Sound eye; (▨) affected eye.

subject JLB. There was no drift of the sound eye except in subject MB, who showed a backward drift of the sound eye. Drifts of each eye in this subject were in opposite directions, converging the eyes onto the target. In *centripetal to sound-side gaze movements* (Fig. 6D; see example Fig. 4D), there was no drift of the sound eye because of the accuracy of the saccade. The affected eye showed a backward drift to correct the position error of the eye after an overshooting saccade.

DISCUSSION

Strabismus, the misalignment of the two eyes, is of mostly unknown etiology. DRS is a special form of strabismus for which the etiology of abnormal horizontal eye motility is well-defined as a congenital peripheral motor deficit (absence of the sixth motoneuron). Only a few reports have measured saccadic eye movements in this syndrome.[18–22] Most of the studies used electro-oculography and included diverse clinical patterns of DRS (types I, II, and III), described eye movements only qualitatively, and made no distinction between centrifugal and centripetal movements. Our study focused on saccade properties in patients with unilateral DRS type I who showed similar deficits on clinical examination.

Techniques

Accuracy and precision of the high-resolution eye movement recordings permit a detailed description and analysis of saccades and the postsaccadic drifts. To study the metrics and kinematics of saccades, it is essential to analyze centrifugal and centripetal movements separately. Our data (Figs. 4, 5, 6) clearly show that the saccades had drastically different characteristics for each category of movement and for each side of gaze. Merging data without categorizing eye movements can lead to confusing conclusions[22] that contradict previous results. Indeed, the eye moves in the orbit by the contraction of the agonist muscle and the relaxation of the antagonist muscle. This has been quantified by Collins et al.,[23] who measured the relative contribution of agonist and antagonist muscles during saccades. The relative contribution of relaxation of the antagonist is mostly important in centripetal movements. For instance, when saccades to the sound side are considered, it is evident that centrifugal and centripetal saccades must be separated in DRS, because the initial position of the two eyes is different for centripetal movements, whereas it is the same for centrifugal movements.

Saccadic Innervation

To move the eyes rapidly despite the viscous drag of the orbital tissues, the eye muscles must develop a large transient force. This force is generated by a high-frequency burst, or pulse, of phasic neural activity. To hold the eye at one point in the orbit, the agonist muscle must maintain tension, to balance the elastic restoring force of the orbital tissues and the antagonist muscle. This sustained force is generated by a step change in tonic activity.[24] The pulse and step of innervation must be adjusted so that the pulse drives the eye to the desired position and the step holds it there. Inappropriate innervations give rise to inaccurate eye movements, and a mismatch between the pulse and the step evokes postsaccadic ocular drifts.

Saccades toward the Affected Side

Saccades of the sound eye are orthometric with no drift. This normal behavior in centripetal and centrifugal direction to affected-side gaze clearly indicates the integrity of the sixth nerve interneurons of the affected side. Saccades of the affected eye are too small and are followed by a smooth postsaccadic onward drift. In the centrifugal direction, this anomalous behavior demonstrates the affected eye's inability to abduct. The pulse of innervation to the affected eye is absent or very low because of the absence of the sixth nerve. The small saccade that is detected comes either from a few residual sixth motoneurons (below the resolution of the MRI) or from relaxation of the restricted antagonist MR muscle. The postsaccadic, smooth, onward drift shows that the step is larger than required to hold the eye still after the saccade. In the centripetal direction, the relaxation of force in the antagonist muscle (MR) largely contributes to the generation of the saccade, which is facilitated by elastic forces driving the eye to the midline (position of "rest"). The saccade amplitude is therefore larger (half of the amplitude of the sound eye) despite the absent or weak innervation from the sixth nerve. The pulse is still insufficient, but the step is adapted and a postsaccadic onward drift compensates for the residual interocular position error and drives the eye to the midline on the target, reaching the position of the SE. The metrics of saccades for each eye in the affected-side gaze are very similar across subjects. Two remarks have to be made concerning results of subject FDR. First, he was the only subject who had esotropia in primary position with inability of the affected eye to reach midline. Therefore, saccades to affected-side gaze in the centrifugal direction corresponded, in fact, to a centripetal movement in the orbit. In addition, the postsaccadic onward drift was absent with the eye restricted to the midline.

Saccades toward the Sound Side

The axial and coronal MRI orbital images of subject MB clearly showed no LR muscle atrophy on the affected eye in primary position (Figs. 3B, 3E). A denervated muscle usually atrophies.[25] Misinnervation or the presence of some innervation of the denervated muscle explains the absence of atrophy. The visualization of LR and MR co-contraction of the affected eye during sound-side gaze movements brought evidence of anomalous innervation of the LR by the ipsilateral third nerve (Figs. 3C, 3F). The innervation for gaze to the sound side is presumed normal, with a common pulse (conjugate drive signal, described later) sent to the two eyes. The velocity of the saccade of the affected eye is much lower than in the sound eye, because there is a large difference in initial orbital position of the two eyes. The contribution of the relaxation of LR muscle is much larger in the sound eye. The size of the pulse seems to be adapted to the sound eye, and consequently there is a slight but consistent overshoot of the target by the affected eye that is compensated for by a backward drift. In the centrifugal direction, paradoxical co-contraction of MR and LR muscles of the affected eye from the third nerve may explain a slower and shorter saccade of the affected eye. The step of the affected eye is adapted with an onward smooth postsaccadic drift to correct saccade undershoot. In subject MB, the sound eye showed an unexpected overshooting saccade followed by a smooth backward drift (Fig. 4B). It seems that the affected eye's behavior influenced the sound eye, and the system adapted the pulse to have both eyes on target as quickly as possible. This particular behavior may reflect a strategy of compromise of the system to get the two eyes on the target with an optimal time course. It implies an adaptation of the oculomotor pathway with a pulse adapted to the "cyclopean" eye and drifts in opposite directions in the two eyes.

Binocular Control of Saccades

The abducens nucleus contains both motor neurons and interneurons. The abducens motor neurons innervate the ipsilateral LR muscle, and the abducens interneurons cross over and drive the contralateral third nucleus, which innervates the MR muscle of the eye on its side. To illustrate the peripheral oculomo-
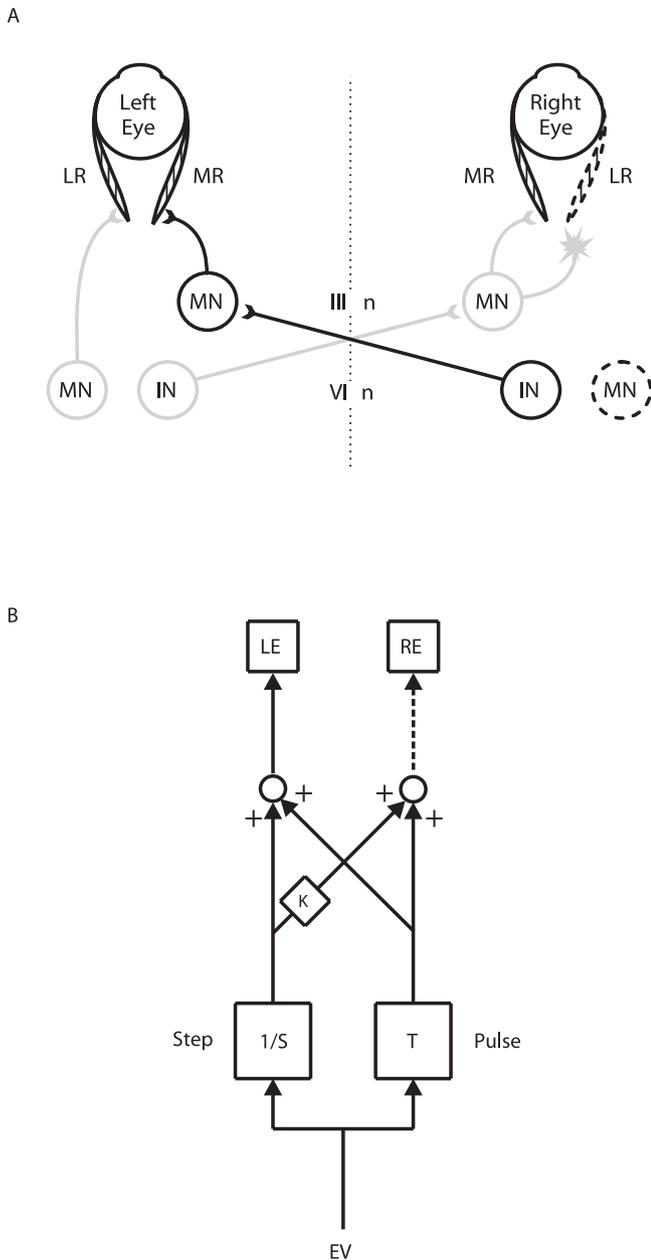
A

B

FIGURE 7.   (A) Brain stem circuitry at the level of peripheral innervation (third and sixth nerve) is drawn as adapted to DRS type I. *Black* denotes active innervation and *gray* inhibited innervation for gaze to the right (affected-side gaze). The axon of the sixth nerve was absent on the right side. *Dotted lines*: motoneuron. Supply of innervation from the third nerve to the LR of the affected is drawn with a star-shaped connection ending. (**B**) A common innervation of the two eyes. The innervation results from an association between the pulse and the step.. The step sent to the affected eye is adapted through gain K.

tor innervation in DRS, a brain stem circuit is drawn in Figure 7A. For example, to move the eyes to the right, the right sixth and the left third nerves have to be excited, but we know from MRI and autopsy studies that the sixth nerve and sixth nucleus motoneurons on the right side are absent in unilateral right DRS type I (subject MB in our study; Fig 2). However, the interneurons on the right side are intact, as shown in previous eye movement recordings and confirmed by our results. This allows a movement of the sound eye to the right. EMG studies have shown innervation from the ipsilateral third nerve to the LR of the affected eye in DRS patients. This anomalous inner-

vation leads to co-contraction of the MR and LR of the affected eye in sound-side gaze, as confirmed in our MRI images (Fig. 3).

The source of the neural command to make a conjugate saccade is somewhat controversial. Neurophysiological and clinical evidence supports Sherrington's law of reciprocal innervation (the agonist–antagonist pair should have opposite changes in innervation), and Hering's law of equal innervation (equal innervations are sent to yoked muscles, i.e., the left LR and the right MR) for extraocular muscles. However, recent studies[26,27] have found evidence that some premotor neurons that should encode binocular commands may actually encode monocular commands. Based on these findings, King and Zhou[28] proposed a model of monocular premotor control of disconjugate saccades. In addition, abnormalities producing disconjugate eye movements have been reported and discussed within the framework of independent control of each eye.[29] Unilateral congenital aplasia of the sixth nerve makes DRS an excellent disease for studying the independent control of the two eyes. Indeed, many characteristics of the congenital deficit (the different mechanical properties of the two eye plants and the normal sensorial status) would give independent motor commands a significant advantage in controlling eye movements in patients with DRS. However, our results are more consistent with the classic hypothesis that both eyes receive the same conjugate drive signal. For each category of eye movements (Figs. 4A–D), adaptation of the step was independent in the two eyes (Fig. 7B), because the postsaccadic drifts always drive the eyes toward the same final position. If the step were the same in both eyes, the final position of the normal and affected eyes would be different for some categories (e.g., the affected eye retracts during adduction because the LR is not relaxing enough to obey Sherrington's law, so the step in that eye must adapt to compensate). In contrast, independent adaptation of the pulse, however desirable in DRS, never occurs, because there is a systematic overshoot (in centripetal direction) or undershoot (in centrifugal direction) of the affected eye in sound-side gaze. Thus, the pulse command must either be common to the two eyes (Fig. 7B), or the two monocular pulses must not be independently adaptable (in which case, there seems little reason to have two monocular pulse generators).

Patients with DRS provide an excellent clinical example for studying fundamental questions about oculomotor control. In the present study, the results in DRS patients support the binocular, but not monocular, theory of saccadic drive. Our results also provide evidence that the steps of innervation for the two eyes are independently controllable. Our results also suggest that the anomalous innervation to the LR of the affected eye from the ipsilateral third nucleus has some practical benefits for the subject. If the LR were simply denervated, its mechanical properties (e.g., stiffness) would undergo significant changes. This would destroy the conjugacy of movements in which the LR is both agonist and antagonist. However, if the anomalous innervation from the third nerve could maintain the mechanical properties of the muscle, then the loss of the sixth nerve would have very little effect on its action as an antagonist. If adaptation could account for the increase of antagonist force on sound-side gaze, binocularity could be maintained in at least one hemifield. Further investigation of other types of DRS should be undertaken in the future to explore adaptation when the clinical picture is more complex.

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