Pergamon

0042-6989(94)E0045-M

*Vision Res.* Vol. 35, No. 1, pp. 109–116, 1995
Elsevier Science Ltd. Printed in Great Britain

# Ocular Motor Abnormalities in Achiasmatic Mutant Belgian Sheepdogs: Unyoked Eye Movements in a Mammal

L. F. DELL'OSSO,*† R. W. WILLIAMS‡

*Received 20 December 1993; in revised form 15 February 1994*

**We studied the eye movements of several members of a family of Belgian sheepdogs that includes achiasmatic mutants. Our aim was to identify the types of nystagmus and other ocular motor abnormalities exhibited by the mutants. We also recorded from several unaffected heterozygous carriers of the genetic mutation and from a normal Irish Setter. Mutant dogs exhibited nystagmus waveforms that were occasionally similar to those of humans with congenital nystagmus (CN). Foveating and braking saccades and foveation periods were seen in some waveforms. More common were pendular oscillations of both eyes that were essentially independent in amplitude and phase. At some times there was a pendular nystagmus with a 180 deg phase shift between the movements of the eyes. Similar to the nystagmus, saccades were often unyoked or uniocular. The eye movements of unaffected relatives did not reveal any saccadic instabilities. However, small saccadic intrusions could have been masked by quantization artifacts. Individual dogs from this family provide an animal model of the ocular motor consequences of the disturbed visual input caused by the absence of an optic chiasm and a novel model of CN. Despite any other ocular motor abnormalities present, the CN may be studied in isolation just as in humans it is studied when strabismus and other types of nystagmus are present. Further studies of ocular motor development and function in achiasmatic dogs have the potential to reveal both the organization of the control systems for *each* extraocular muscle and the role of yoking of the agonist muscles of the two eyes.**

Congenital nystagmus    Uniocular saccades    Achiasmatic misrouting

## INTRODUCTION

Analysis of the causes and treatment of congenital nystagmus (CN) has been hampered by the lack of an animal model of this common human ocular motor abnormality. Notable efforts by Tusa *et al.*, involving alternating monocular deprivation in immature primates have succeeded in generating animals with several syndromes including nystagmus similar to human CN or latent/manifest latent nystagmus (LMLN) (Tusa, Repka, Smith & Herdman, 1991). However, the procedures are difficult and the nystagmus is an imperfect model because it must be generated experimentally. In recent work, we have raised the possibility that a recessive mutation carried in Belgian sheepdogs may provide a viable animal model of human CN (Williams, Garraghty & Goldowitz, 1991; Williams & Dell'Osso, 1993). Because the syndrome is truly congenital, these animals may be of use in the long term for testing treatments to minimize or eliminate nystagmus from early stages of development.

Belgian sheepdogs with pronounced horizontal nystagmus were first observed by de Lahunta and Cummings (1974) at Cornell University. Necropsies of three siblings with pendular (unrecorded) nystagmus revealed a complete failure of optic axons to decussate at the optic chiasm (de Lahunta, personal communication). The eye movement disorder reemerged in close relatives of the first litter more than one decade later and intense efforts over 5 yr have lead to the establishment of a breeding colony of sheepdogs with pronounced nystagmus (Williams *et al.*, 1991).

In this report we provide an initial characterization of the ocular motor abnormalities in these dogs and in normal littermates. Our goal in this study has been to assess the degree to which the ocular motor abnormalities of these dogs resemble or differ from human CN. Our work has been directed at determining whether these

---

*To whom all correspondence should be addressed at: The Ocular Motor Neurophysiology Laboratory, Veterans Affairs Medical Center (127A), 10701 East Boulevard, Cleveland, OH 44106, U.S.A.

†Departments of Neurology and Biomedical Engineering, Case Western Reserve University, 2040 Adelbert, Cleveland, OH 44106 and University Hospitals of Cleveland, Ohio, U.S.A.

‡Department of Anatomy and Neurobiology, University of Tennessee, Memphis, TN 38103, U.S.A.

animals will be useful in understanding the causes of CN and in testing potential treatments for CN in humans. The recent, exciting discovery by Apkarian, Barth, Wenniger-Prick and Bour (1993) of humans with an atypical nystagmus associated with elimination of the crossed retinal projection at the chiasm, has also motivated us to closely compare the eye movements in achiasmatic dogs with those described in these humans. In a concurrent study of the topography of retinal projections in achiasmatic mutant dogs (Williams, Hogan & Garraghty, 1995), we have discovered highly unusual mirror-image maps in the dorsal lateral geniculate nuclei of dogs with nystagmus. This finding enables us to develop a provisional model of the anatomical and physiological substrates that may underlie the highly unusual types of unyoked, disconjugate saccadic eye movements described in this paper.

## METHODS

The Belgian sheepdog is a moderate-sized dog (20–30 kg) with a solid black coat and normally pigmented eyes. The Belgian sheepdogs whose eye movements are the subject of this study come from a family that includes mutants whose optic chiasms have not formed (Fig. 1). We have isolated an autosomal recessive mutation in a family of these dogs in which the entire retina projects to the ipsilateral side of the CNS. The achiasmatic mutation displays a pattern of misrouting of optic axons opposite to that seen in albino mutants, in which an excess of fibers cross at the chiasm (Collewijn, Apkarian & Spekreijse, 1985; Apkarian, Reits, Spekreijse & Van Dorp, 1983; Apkarian & Shallo Hoffman, 1991). Clinical examination of the mutant dogs in this family reveals a striking nystagmus, head turns and behavior that are absent in their unaffected relatives. This behavioral complex is similar to that seen in some human albinos and the recently described human achiasmatics (Apkarian *et al.*, 1993, 1995). All applicable NIH. guidelines and regulations regarding the care and handling of the dogs are followed at the kennel and were adhered to in this study.

### *Recording*

Horizontal eye movement recordings were made using a mobile system employing the infrared (IR) reflection method. The IR system bandwidth was 0–100 Hz. Eye position signals were digitized on-line at 250 samples/sec and displayed by a Tektronix TDS 420 digitizing oscilloscope. The oscilloscope was interfaced to a Macintosh IIci via a IEEE 488.2 protocol. Data files for each 20-sec (5000 samples) recording interval were stored in ASCII format with 8-bit resolution for later analysis.

### *Protocol*

Eye movements were recorded in a quiet examination room at the kennels where these untrained dogs are housed. For most records, the dogs fixated on the face of the person holding the IR frame to their eyes. This procedure is similar to that used to record from human infants (see below). We also tried to direct the dogs' attention to a more distant face straight ahead and in lateral gaze. The recording session was the dogs' first exposure to the apparatus and the first attempt to record dog eye movements by the authors. Thanks to the cooperative nature of these dogs, we were able to obtain eye-movement records from all dogs but one without the use of sedatives. One dog required 0.2 cm$^3$ of Rompun in order to obtain records; a similar dose was given to a dog previously tested without drugs to reveal any effects of the drug on the nystagmus. The absence of a chiasm in the mutant dogs has been verified by anatomical post-mortem studies. All mutant dogs with nystagmus in this family who have been studied anatomically, either lacked a chiasm or, in one case, had a severely maldeveloped chiasm. One of the dogs from this study (M3) has since been studied anatomically and the absence of a chiasm verified. During this ocular motor study, we recorded from four homozygotes, two heterozygotes and one normal dog from this family plus one normal Irish Setter.

For this preliminary study, the eye movements of the dogs were recorded using a technique we developed for infants to obtain accurate waveform and interocular

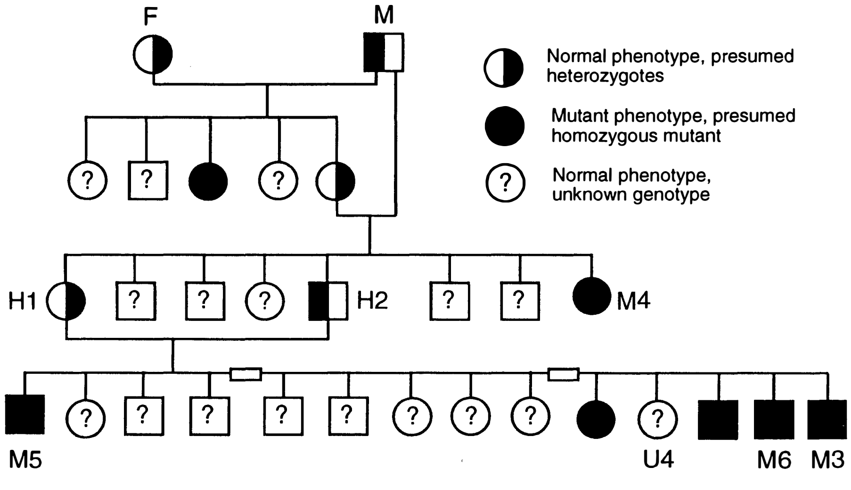

FIGURE 1. Pedigree of achiasmatic dogs. We recorded from the identified animals in the lower two generations.

phase information without absolute amplitude calibration. The IR apparatus (with spectacle frames) was held firmly in front of the dog after proper setting of the interpupillary distance. The experimenter's hands were placed along the temples with both thumbs on the muzzle of the dog to help stabilize the head and provide three-point stability for the IR structure with respect to the head. Despite the fact that the dogs were untrained, this method produces accurate binocular records of the waveforms of dogs that make possible the diagnosis of the particular type of nystagmus present. Each dog was held by one of the authors while the other held the IR electronics frame in front of the animal. During testing, the dogs allowed us to hold their heads still for most of each record. If the dog moved his head upwards during the 20-sec recording interval, only the data collected before the movement was used. Using this protocol, we obtained 28 recordings with an average record length of 16.8 ± 2.8 sec. Our techniques produced neither pain nor discomfort in the dogs. Once the dogs are trained to fixate LEDs at known gaze angles while their head are restrained, we will be able to calibrate the eye movements for future studies.

### *Analysis*

Before analysis, all data files were digitally low-pass filtered using either a five-point, weighted moving average filter or a Hamming window to reduce the quantization noise produced by the 8-bit resolution of our mobile system. Future acquisition of a higher resolution mobile system is planned. Depending on the level of quantization noise in a particular record, typical Hamming windows had widths of 99 or 51 samples at respective cutoff frequencies of 50 to 18 Hz. Both moving average and Hamming filters produced acceptable data for analysis without distorting the CN waveforms. Slight movements of the IR electronics frame might also have produced noise that added to the quantization noise. We conducted tests to determine the effects of possible frame movements on the eye-movement records. Horizontal, vertical and in/out movements produced directionally conjugate deflections of the traces of *both* eyes whereas clockwise or counter-clockwise movements produced oppositely directed displacement in *both* traces. No artifacts could be induced in one eye channel only. Occasionally, movement caused by panting would produce a conjugate, pendular noise signal at the respiratory frequency (approx. 5 Hz). Frame movements, regardless of their source, increased the difficulty of identifying small foveating or braking saccades. During preliminary analysis of each record, all blinks and movement artifact were identified and marked. Only those eye movements undistorted by either blinks or movement artifact were analyzed. CN waveforms and saccades were then identified using both eye position and velocity records.

An approximate indication of the amplitudes of the dogs' nystagmus was obtained by post-calibrating the records taken using a record made of a human with CN of known amplitude. The human record was made during the recording session in the kennel with all instrument settings unchanged and with the same protocol for positioning the IR frame. If placement of the IR frame was not equidistant from both eyes for a particular recording interval (indicated by a gain asymmetry in the two records), an additional adjustment was made to equalize the gains. The scales shown in all figures in this report are based on this derived calibration procedure. Data analysis (and filtering, if required), statistical computation of means and standard deviations, and graphical presentation were performed on an IBM PS/2 Model 80 using the ASYST software for scientific computing. Eye velocities were obtained by digital (two-point algorithm) differentiation of the position signals. Further details on ASYST may be found elsewhere (Hary, Oshio & Flanagan, 1987).

## RESULTS

Prior to eye-movement recording, we videotaped the eye movements of several mutant dogs. Examination of the videotapes revealed nystagmus that was at times disconjugate, a vertical see-saw component in some segments, and the occurrence of seemingly uniocular saccadic eye movements. We then recorded the eye movements of three male mutants (M3, M6 and M5) and one female mutant (M4) to determine if the clinically visible nystagmus was CN or some other type of nystagmus. Two of the males (M3 and M6) were litter mates (Fig. 1). We also recorded the eye movements of one male (H2) and one female (H1) of normal phenotype but proven to be heterozygotes, and one female (U4) of normal phenotype but unknown genotype, to determine if there were any subclinical ocular motor abnormalities present in relatives of the mutants.

### *Eye movements of mutants*

Both preliminary clinical observation and video tapes of the mutants' eye movements revealed a marked nystagmus. With the exception of M6, the mutant dogs' nystagmus and their head turns and tilts presented clinical pictures resembling those of human CN.

M3 appeared to have a circular-elliptical nystagmus of intermediate amplitude and low frequency. He had a left head turn and also a counter-clockwise head tilt (defined from the dog's point of view). Recordings of M3's eye movements contained nystagmus waveforms similar to those seen in human CN (Dell'Osso & Daroff, 1975). Pendular (P), pendular with foveating saccades ($P_{fs}$), jerk with extended foveation ($J_{ef}$), and pseudopendular with foveating saccades ($PP_{fs}$) were recorded. Peak-to-peak amplitudes ranged from < 1 to 8–10 deg with frequencies of 2–5 Hz. Figure 2(a) contains $P_{fs}$ waveforms plus a 5 Hz "panting" artifact. Figure 2(b) shows a period of disconjugate P oscillations and a uniocular saccade of approx. 6 deg. The quantization noise (0.2–0.4 deg) should be ignored.

M6, on the other hand, appeared to have a high-frequency, flutter-like, low-amplitude oscillation that did not seem to be conjugate. M6's eye movement records

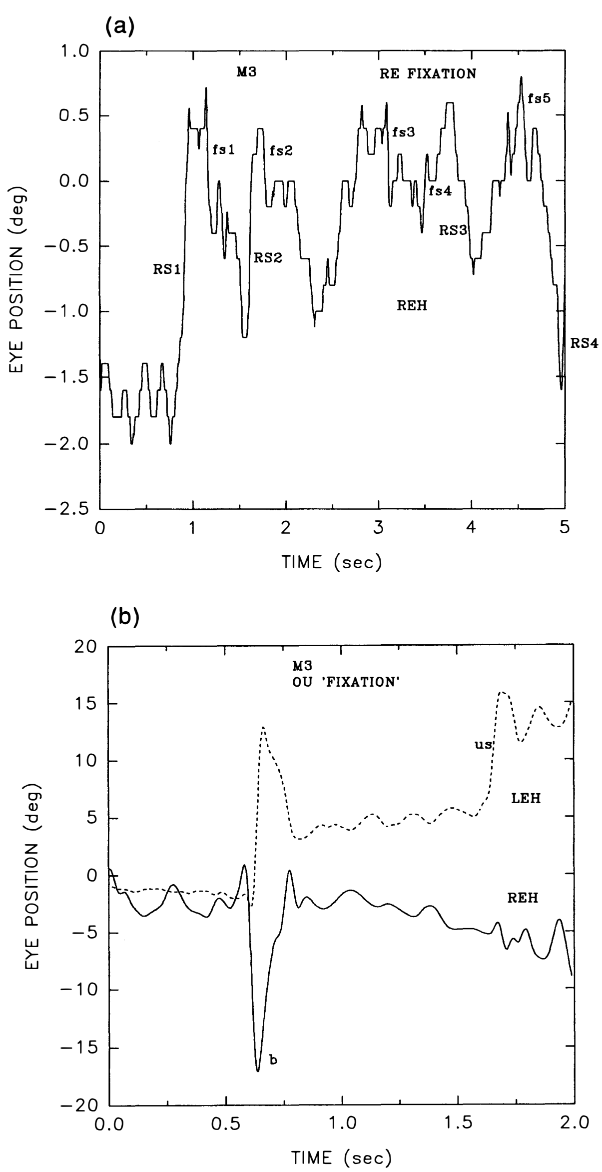

FIGURE 2. M3's eye movements showing $P_{fs}$ waveforms in (a) and disconjugate P waveforms in (b). In this and succeeding figures, rightward eye positions and movements are positive and leftward are negative. RS, refoveating saccade; fs, foveating saccade; bs, braking saccade; us, uniocular saccade; s, saccade (conjugate); cs, convergent saccade; ds, divergent saccade; REH, right eye horizontal; LEH, left eye horizontal; b, blink.

contained a 9–10 Hz, low-amplitude (0.2–3 deg) P oscillation that usually was unyoked in both amplitude and phase but sometimes appeared phase-locked in phase or 180 deg out of phase in the two eyes [see Fig. 3(a)]. In addition, there was an occasional slow (0.8 Hz) vergence oscillation upon which the 9–10 Hz P oscillation was superimposed. The records contained numerous uniocular saccades of both eyes in both horizontal directions. Some uniocular saccades were >30 deg in amplitude [Fig. 3(b)].

M4 appeared to have a see-saw component to her large-amplitude, low-frequency nystagmus. M4's eye movements were also distinctive for their large (15 deg) saccades as is illustrated in Fig. 4(a). The right eye exhibited large uniocular saccades following the disjunctive saccade shown at approx. 0.1 sec on the time axis. During these uniocular saccades, the left eye either drifted or was relatively stationary.

M5 had an intermediate-amplitude, low-frequency nystagmus with both vertical and horizontal components. He had a right head turn with a clockwise head tilt. M5's eye movements contained P waveforms and saccades that were either conjugate, uniocular or directionally disconjugate. Figure 4(b) contains all three types of saccades: conjugate at approx. 0.4 sec; convergent at 0.7 sec; and several uniocular saccades throughout the rest of the figure.

### *Eye movements of a normal dog*

To have a standard of comparison of the saccades of the non-mutant dogs, we also recorded the eye movements of a normal Irish Setter (B1). He exhibited conjugate saccades whose velocity profiles resembled

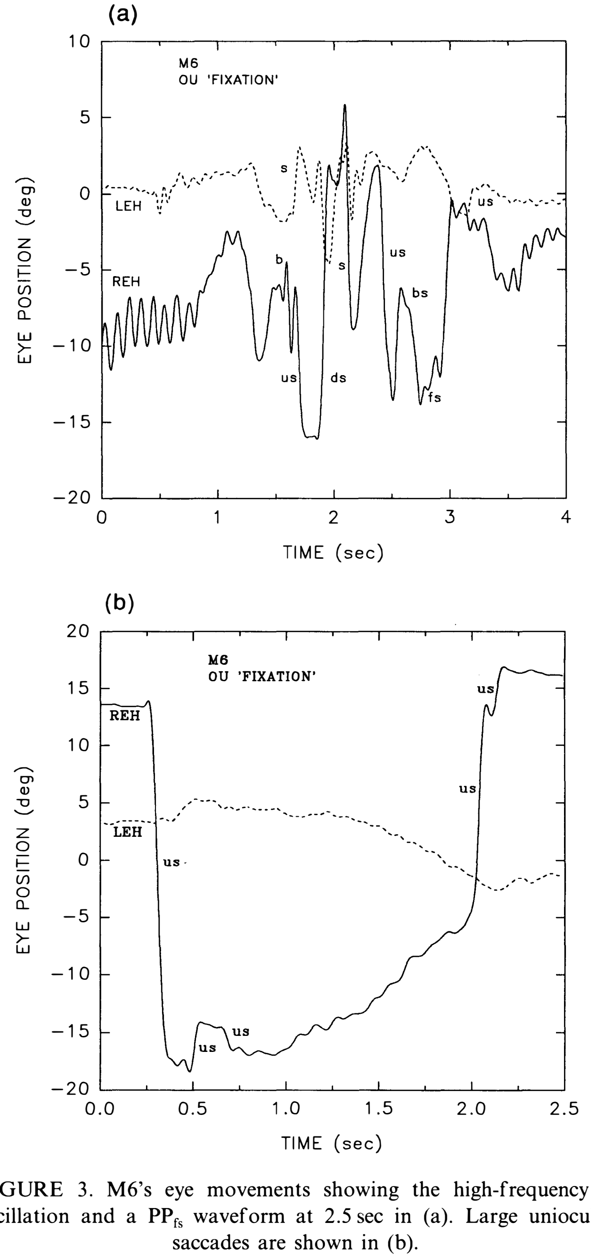

FIGURE 3. M6's eye movements showing the high-frequency P oscillation and a $PP_{fs}$ waveform at 2.5 sec in (a). Large uniocular saccades are shown in (b).

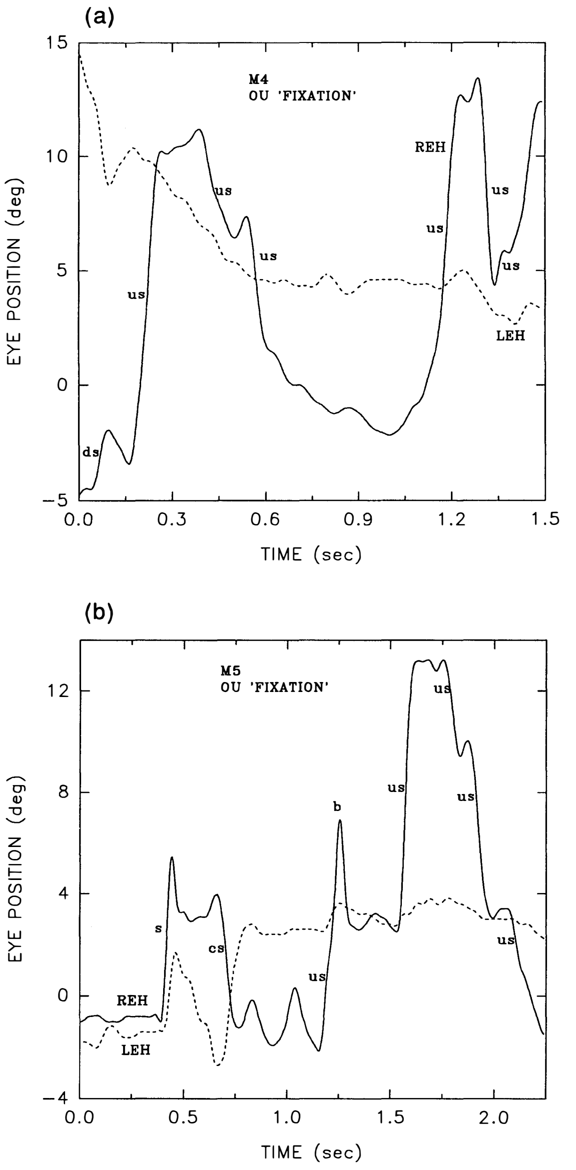

FIGURE 4. (a) M4's eye movements containing large uniocular saccades and a divergent saccade. (b) M5's eye movements containing conjugate, convergent and uniocular saccades.

those of human saccades. Figure 5 shows the conjugate nature of B1's saccades with a slight inter-eye timing difference. One record also contained a pair of oppositely directed saccades separated by 350 msec that resembled the square-wave jerks seen during human fixation.

### *Eye movements of heterozygotes*

Examination of the phenotypically normal, heterozygote dogs (H1 and H2) did not reveal any clinically evident nystagmus. Their eye movement recordings contained conjugate saccades resembling those of B1 (the normal Irish Setter) and of humans; no nystagmus was found. Figure 6 shows the conjugate nature of H1's saccades and the loose inter-eye precision in the timing of these saccades. Occasional, slow drifting (0.4–0.6 deg) of the right eye can also be seen. Such vergence drifts were common in the records we made from non-mutant dogs.

### *Eye movements of unknown genotypes*

Examination of U4, a dog of normal phenotype but unknown genotype, revealed no clinically evident nystagmus. Eye movement recordings contained normal, conjugate saccades and no nystagmus. Thus, the movements of this normal dog, the heterozygotes and the Irish Setter were indistinguishable and did not contain large uniocular saccades.

## DISCUSSION

In humans there are a variety of non-symptomatic types of infantile nystagmus possible. In addition to CN, they include LMLN, the dissociated pendular nystagmus of spasmus nutans and the combination of CN and LMLN seen in the nystagmus blockage syndrome (Dell'Osso, 1993). By recording the eye movements of both mutant and non-mutant dogs from this family, we attempted to answer some of the questions about: the type of nystagmus the mutants had; the relationship of the nystagmus to the lack of fiber crossing; similarities to the CN seen in most human albinos; the degree of normal or abnormal (other than the nystagmus) ocular motor behavior resulting from this severe chiasmal defect; and the extent to which the non-mutant dogs exhibited subclinical, abnormal eye movements. Some of our findings were reported at the 1993 Spring Meeting of AVRO (Williams & Dell'Osso, 1993).

### *Anatomy of the mutant visual pathway*

In many vertebrates (e.g. fish, frog, lizard or bird), virtually all retinal fibers cross (decussate) at the optic chiasm. In mammals, a variable and often large percentage of fibers remain on the same side; this is referred to as a partial decussation. About 55% of the fibers are crossed in humans, many additional fibers cross in

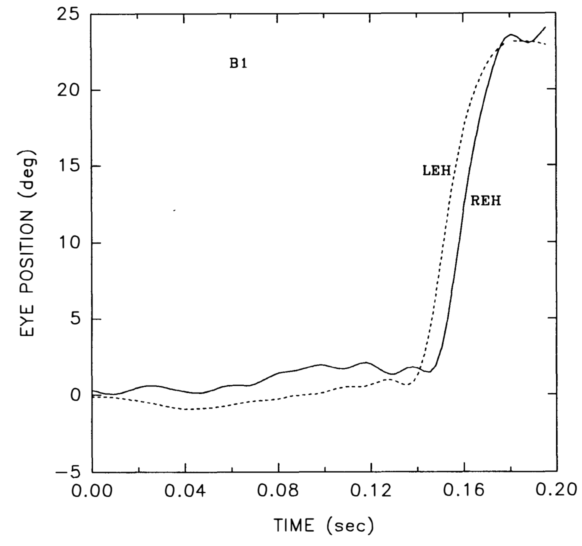

FIGURE 5. B1's eye movements showing the conjugate nature of his saccades and the imprecise yoking seen as an inter-eye time difference.

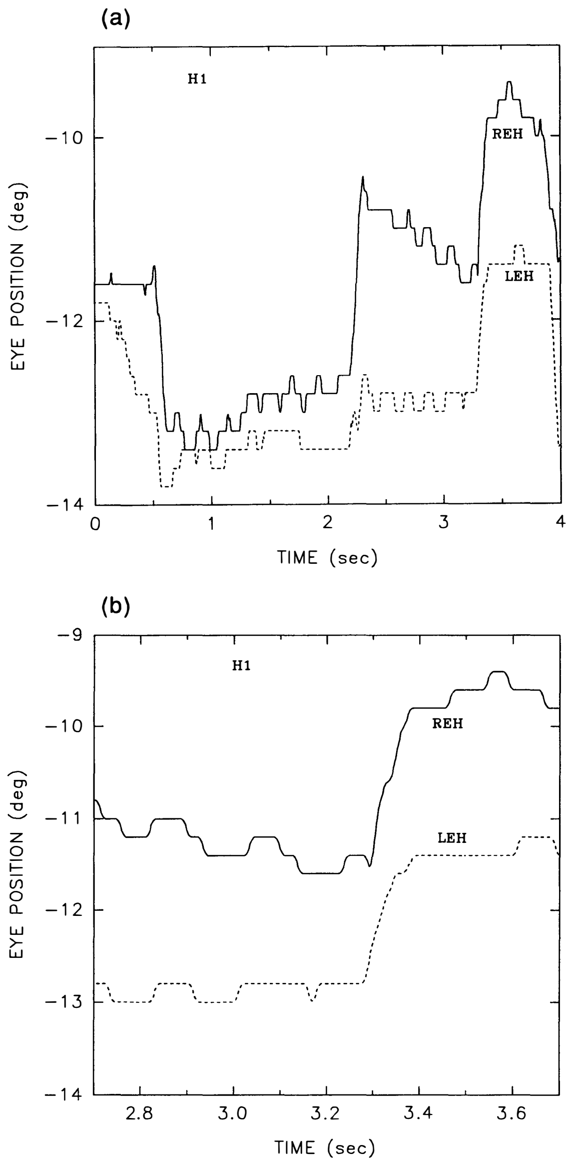

FIGURE 6. H1's eye movements showing (a) conjugate saccades and (b) an expanded time scale portion of one of the saccades demonstrating the imprecise yoking seen in this dog.

human albinos, and in normal dogs, about 80% of their optic nerve fibers cross. The absence of an optic chiasm in the mutant dogs we tested, forces the optic nerve fibers into the ipsilateral optic tract; according to a definitive text on the vertebrate visual system, "... no such condition is on record in Vertebrates" (Polyak, 1957). In terms of crossed and uncrossed optic fibers, achiasmatic dogs represent a condition opposite to many lower vertebrates (e.g. chameleons with a totally crossed retinal projection) and almost opposite to human albinos. In a sense, they are "anti-chameleons" and almost "anti-albinos".

The normal dog has binocular vision, an area centralis, and optic fibers meant to decussate only partially at the optic chiasm and synapse in specific layers of both the ipsilateral and contralateral lateral geniculate nuclei (LGN) and then project to the ipsilateral visual cortex. The large size of an area centralis, relative to a fovea, may be responsible for the vergence drifts seen in the recordings of normal dogs. It is not immediately obvious what the visual world looks like to such an animal when a mutation prevents the partial decussation at the chiasm. Fibers from the temporal retina of each eye correctly synapse in the LGN but the fibers from the nasal retina terminate with a reversed polarity in the ipsilateral LGN and project inappropriately into the ipsilateral visual cortex. If some form of adaptation to the congenitally misdirected nasal input takes place, the information within each hemicortex could be properly interpreted to allow correct perception of the whole visual field. The dogs' ability to direct their fixating eyes toward lateral stimuli and to navigate suggests that some adaptation has taken place and that each eye is capable of providing a usable representation of its visual field. Of course, these animals are unlikely to have any form of binocular vision.

### *Relation to human albinism*

The achiasmatic dog, having no decussating retinal fibers, has a defect opposite to that associated with albinism in humans and other vertebrates, an excess of retinal fibers decussate at the chiasm. These two deficits, with opposing visual effects, are associated with the occurrence of CN in the developing ocular motor system. This should not be a surprise since other so-called afferent defects have also been linked to CN. Among them are aniridia, astigmatism, foveal a(dis)plasia, and congenital cataracts. It should be noted that these are *aplanar* sensory deficits and that CN is mainly an uniplanar (horizontal motor deficit. This observation provides evidence against any of these sensory defects being the direct cause of CN. The deficit caused by excess decussation in albinism is a horizontal deficit but if too many crossing fibers cause CN by a putative sign reversal, as has been suggested, how can the achiasmatic condition (where there are *no* crossing fibers) also cause CN? Most humans with CN are not albinos and do not have excess crossing fibers (Apkarian & Shallo-Hoffman, 1991; Shallo-Hoffman & Apkarian, 1993). The addition of the achiasmatic syndrome to the list of afferent deficits associated with CN supports the hypothesis that most developing ocular motor systems required good visual input to be properly calibrated and *any* sensory deficit present in infancy may be sufficient to perturb such calibration and thereby result in CN. The prevalence of horizontal CN may merely represent the propensity of horizontal system oscillation over a less-important vertical system. Thus, although such sensory deficits may encourage oscillations to develop, they are not the *direct* cause of CN. Only the combination of system gain and loop delay necessary for such oscillations can be their direct cause, whether or not any sensory deficit is present; the existence of many cases of idiopathic CN demonstrates this conclusively.

### *Relation to achiasmatic humans*

Two cases of achiasmatic humans have recently been described (Apkarian *et al.*, 1993, 1995). Both VEP and

MRI findings established the absence of any chiasmal decussation in these patients. In these patients, nystagmus was clinically evident and, when recorded, exhibited CN typical waveforms (predominantly $P_{fs}$, P, pseudocycloid, and $J_{ef}$) and a vertical see-saw component. Thus, absence of decussating retinal axons can be added to the above list of human sensory deficits associated with, but not the direct cause of, *human* CN.

### *Animal model for CN*

Monkeys subjected to early monocular deprivation of vision developed strabismus, LMLN, and some CN waveforms (Tusa *et al.*, 1991). Although that paradigm did not duplicate the human conditions preceding CN, the resulting nystagmus may be useful in studying CN. There currently are no animal models for human CN uncomplicated by other types of nystagmus. Similarly, the achiasmatic syndrome is not the common precondition for human CN. However, since the nystagmus seen in these mutant dogs is CN, rather than some other form of nystagmus (or a combination of two or more forms), they also represent an animal model. The presence of braking (Dell'Osso & Daroff, 1976) and foveating saccades and of foveation periods is pathognomonic of CN. The waveforms we documented in these achiasmatic dogs (P, $P_{fs}$, $J_{ef}$, and $PP_{fs}$) are typical CN waveforms (Dell'Osso & Daroff, 1975) and, with the exception of P, have not been recorded in any other form of nystagmus. The major difference between the nystagmus present in achiasmatic dogs and that of humans with CN is the presence of uniocular nystagmus and the lack of phase conjugacy between the movements of the two eyes. It remains to be determined if either of these characteristics is exhibited by the human achiasmats.

This study presents the first documentation of periods of extended foveation in a non-human nystagmus waveform. It has been hypothesized that, in humans, such period are: the result of the fixation system's attempts to maintain steady fixation in the presence of the nystagmus oscillation (Dell'Osso & Daroff, 1975); necessary for good acuity (Dell'Osso, Flynn & Daroff, 1974; Dell'Osso & Daroff, 1975; Dell'Osso, Van der Steen, Steinman & Collewijn, 1992); and necessary for the suppression of oscillopsia (Dell'Osso & Leigh, 1992a, b). In these achiasmatic dogs, we recorded periods of extended foveation in the CN waveforms of one eye while the other seemed to be drifting without any obvious attempt by the ocular motor system to maintain precise eye position. We interpret this as a reflection of fixation by one eye at a time and the concurrent release of accurate control of the other. This mimics the loose control seen in the strabismic eye of humans with uniocular fixation. We hypothesize that periods of extended foveation are imposed on the dogs' CN waveforms for the same reasons as in humans, although we cannot prove that the dogs do not have oscillopsia. We can only report that their abilities to navigate within their environment suggest that they, like their human counterparts, suppress the oscillopsia that would normally accompany nystagmus.

Given the CN in these dogs and the hypothesis that human CN is a disorder waiting to happen, achiasmatic dogs represent an animal model in which anatomical, physiological, behavioral and therapeutic studies of the CN can be carried out. The presence of other ocular motor abnormalities associated with achiasma provides opportunities for their study as well but does not preclude the study of CN.

### *Ocular motor organization*

Current models of the ocular motor system in binocular vertebrates generally impose or assume a tight yoking of the two eyes, using the *same* elements to control the movements of *both* eyes in each direction (i.e. one pulse generator and one neural integrator for both eyes in each direction). Such models presuppose corresponding neuroanatomical substrates on each side of the brain stem. However, they cannot easily produce uniocular saccades, uniocular nystagmus, or directionally opposed saccades. We presume that the ocular motor systems of dogs are similar to those of monkeys and humans and normally make conjugate movements to maintain binocular single vision. However, in the achiasmatic dogs we found both uniocular saccades and uniocular oscillations. This implies that the neuroanatomical substrate for independent control of each eye might already be present in these animals. That is, there may exist anatomically separate populations of burst neurons for each eye on each side of the brain stem and they synapse with anatomically separate populations of neural integrator neural networks on their respective sides of the brain stem. Normally these populations would be yoked and fire in synchrony to produce conjugate eye movements but, when yoking fails to develop, each population might be able to fire independently to innervate its respective eye muscle and move its respective eye in a desired direction.

## REFERENCES

Apkarian, P. & Shallo-Hoffman, J. (1991). VEP projections in congenital nystagmus; VEP asymmetry in albinism: A comparison study. *Investigative Ophthalmology & Visual Science*, *32*, 2653–2661.

Apkarian, P., Bour, L. & Barth, P. G. (1995). A unique achiasmatic anomaly detected in non-albinos with misrouted retinal-fugal projections. *European Journal of Neuroscience*. In press.

Apkarian, P., Barth, P. G., Wenniger-Prick, L. & Bour L. (1993). Non-decussating retinal fugal fiber syndrome: VEP detection of a visual system abnormality associated with visual loss, nystagmus and aberrant optic chiasm. *Investigative Ophthalmology and Visual Science*, *34*, 711.

Apkarian, P., Reits, D., Spekreijse, H. & Van Dorp, D. (1983). A decisive electrophysiological test for human albinism. *Electroencephalography and Clinical Neurophysiology*, *55*, 513–531.

Collewijn, H., Apkarian, P. & Spekreijse, H. (1985). The oculomotor behaviour of human albinos. *Brain*, *108*, 1–28.

Dell'Osso, L. F. (1993). Congenital and other types of infantile nystagmus: Recording, diagnosis and treatment. In Sharpe, J. A. & Barber, H. O. (Eds), *The vestibulo ocular reflex and vertigo* (pp. 229–247). New York: Raven Press.

Dell'Osso, L. F. & Daroff, R. B. (1976). Braking saccade—A new fast eye movement. *Aviation and Space Environment Medicine*, *47*, 435–437.

Dell'Osso, L. F. & Daroff, R. B. (1975). Congenital nystagmus waveforms and foveation strategy. *Documenta Ophthalmologica*, *39* 155–182.

Dell'Osso, L. F. & Leigh, R. J. (1992a). Ocular motor stability of foveation periods. Required conditions for suppression of oscillopsia. *Neuro-ophthalmology*, *12*, 303–326.

Dell'Osso, L. F. & Leigh, R. J. (1992b). Foveation period stability and oscillopsia suppression in congenital nystagmus. An hypothesis. *Neuro-ophthalmology*, *12*, 165-183.

Dell'Osso, L. F., Flynn, J. T. & Daroff, R. B. (1974). Hereditary congenital nystagmus: An intrafamilial study. *Archives of Ophthalmology*, *92*, 366–374.

Dell'Osso, L. F., Van der Steen, J., Steinman, R. M. & Collewijn, H. (1992). Foveation dynamics in congenital nystagmus I: Fixation. *Documenta Ophthalmologica*, *79*, 1–23.

Hary, D., Oshio, K. & Flanagan, S. D. (1987). The ASYST software for scientific computing. *Science*, *236*, 1128–1132.

Polyak, S. (1957). *The vertebrate visual system* (p. 781). Chicago, Ill.: University of Chicago Press.

Shallo-Hoffmann, J. & Apkarian, P. (1993). Visual evoked response asymmetry only in the albino member of a family with congenital nystagmus. *Investigative Ophthalmology & Visual Science*, *34*, 682–689.

Tusa, R. J., Repka, M. X., Smith, C. B. & Herdman, S. J. (1991). Early visual deprivation results in persistent strabismus and nystagmus in monkeys. *Investigative Ophthalmology & Visual Science*, *32*, 134–141.

Williams, R. W. & Dell'Osso, L. F. (1993). Ocular motor abnormalities in achiasmatic mutant Belgian sheepdogs. *Investigative Ophthalmology & Visual Science*, *34*, 1125.

Williams, R. W., Garraghty, P. E. & Goldowitz, D. (1991). A new visual system mutation: Achiasmatic dogs with congenital nystagmus. *Society of Neuroscience Abstracts*, *17*, 187.

Williams, R. W., Hogan, D. & Garraghty, P. E. (1995). Target recognition and visual maps in the thalamus of achiasmatic mutant dogs. *Nature*. In press.

---

*Acknowledgements*—Our thanks to Drs Alexander de Lahunta and John Cummings for the invaluable help in finding mutants, to Mary Young for aid in setting up a colony of these animals, to Bonnie Belton for care of the dogs and to Nirav Sheth for help in preparing the figures. This work was supported in part by the Office of Research and Development, Medical Research Service, Department of Veterans Affairs (Dr Dell'Osso) and by NEI R01-6627 (Dr Williams).