cyclic-AMP[7] by "push-pull" perfusion of the anterior chamber. We found that the 8-methylthio derivative of cyclic-AMP produces a twofold increase in outflow facility, similar to the results obtained with isoproterenol, perfused in the same manner.[2]

With intraocular delivery, in rabbits, both alpha- and beta-adrenergic compounds increase the outflow of aqueous humor[8, 9] while, in monkeys only compounds with beta-adrenergic activity are effective.[2] We conclude that adrenergic agonists, that can stimulate the synthesis of cyclic-AMP, increase the outflow facility of the eye by a mechanism mediated by this cyclic nucleotide. In man, where the pharmacological mechanisms are not clear, topical epinephrine increases outflow facility when used successfully in the treatment of primary open-angle glaucoma.[10] Therefore, increasing the rate of synthesis of cyclic-AMP may be important to the medical management of glaucoma. Further investigations into compounds that stimulate or potentiate the cyclic-AMP system may provide additional approaches to the treatment of this disease.

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Key words: cyclic-AMP, outflow facility, aqueous humor, intraocular pressure, primate, catecholamines, glaucoma.

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Comparative velocities of different types of fast eye movements in man.

J. A. SHARPE, B. T. TROOST, L. F. DELL'OSSO, AND R. B. DAROFF.

The peak velocity-amplitude characteristics of voluntary saccades and the fast phases of caloric, rotational, and optokinetic (OKN) nystagmus were compared in ten human subjects in both light and, except for OKN, darkness. All these fast eye movements had similar velocities and all slowed in darkness. This study supports the presumption that the identical brainstem firing patterns found in monkeys for all fast eye movements also occur in man.

Fast eye movements (FEM) include voluntary and reflex saccades and the fast phases of nystagmus.[1] In monkey, all types of FEM are produced by identical nuclear[2] and prenuclear[3] burst patterns. There is substantial evidence in both humans[4] and monkeys[3] that the pontine paramedian reticular formation at the level of the abducens nuclei is the final prenuclear generator for all FEM. Although many studies have defined the velocity-amplitude characteristics of voluntary refixation saccades,[5] there is a paucity of information concerning intrasubject comparisons of these saccades with nystagmus fast phases. We are reporting such a study of voluntary saccades and nystagmus fast phases induced by caloric, rotation, and optokinetic (OKN) stimuli performed in illuminated laboratory conditions and, except for OKN, in darkness.

Methods. Ten normal volunteers, aged 25 to 40 (six women and four men), served as subjects. None had used sedatives, hypnotics, stimulants, or anticonvulsants within a week preceding the study. Eye movements were recorded by an infrared reflection device mounted on spectacle frames. Eye position signals were DC coupled to a pen-writing

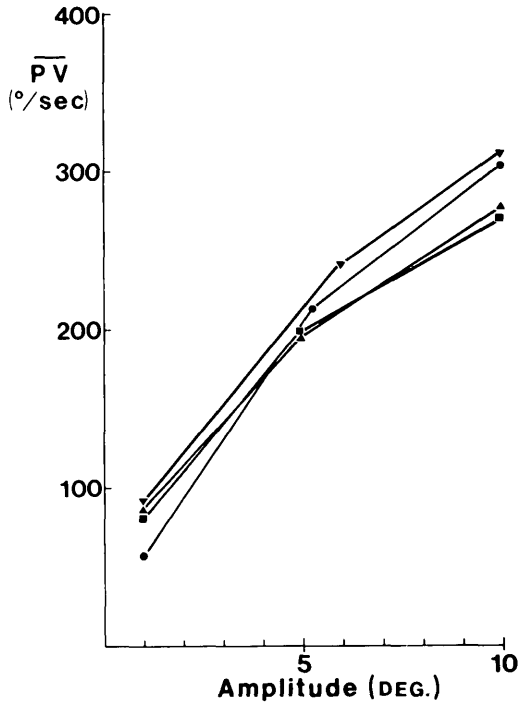

Fig. 1. Mean peak velocity ($\overline{PV}$)—amplitude relationships for FEM in illuminated conditions. Lines represent least mean square fit for all data points between the indicated end points. (●) voluntary FEM, (▲) caloric fast phases, (▼) post-rotary fast phases, (■) optokinetic fast phases.

polygraph with electronic differentiation to yield simultaneous eye velocity. Heads were stabilized by a chin rest and circumferential elastic headbands. The velocity values reflected those of a full system bandwidth of 100 Hz. with a differentiator response time of 4 msec.[5]

We collected FEM data under seven experimental conditions: voluntary saccades between fixed targets and in darkness, OKN, and both post-rotary and caloric nystagmus in normal laboratory illumination and darkness. The recording apparatus was recalibrated before and after each sequence.

Voluntary saccades were elicited by refixations to light-emitting diodes arranged on a horizontal stimulus arc 1.14 m. in radius.[6] We instructed the subjects to alternate fixations between stationary targets separated from 1° to 10°. Saccades in darkness were obtained by asking the subjects to make refixation movements between the previously illuminated lights. To eliminate the complicating factors of drifts and corrective movements which occur in darkness,[7] we only utilized velocity information from the original saccade. We maintained subject alertness by frequent verbal stimulation. The experiments were performed in varying sequence upon different days in individual subjects. OKN was induced by projecting a moving strip of black and white stripes through a translucent screen from left-to-right. Subjects were told to gaze straight ahead and note each stripe. The target speed varied between 3° and 10° per second to obtain nystagmus of varying amplitudes. Post-rotary nystagmus was produced by rotations in a revolving chair at a rate of 180° per second for 30 seconds, following which the chair stopped abruptly. The nystagmus was recorded in the normally illuminated laboratory and in darkness. In the former situation, the nystagmus was always less than 15 seconds in duration which necessitated repeating the procedures several times to obtain sufficient data. Caloric nystagmus, in both light and darkness, was induced with the subject seated in a 60° reclining position and stimulated with ice water irrigation of the right external auditory canal for 30 seconds.

In each experiment, the amplitudes and peak velocity (PV) of leftward FEM of the right eye were determined by visual inspection of the recordings. We can interpret the eye movement analogues with an accuracy of 0.5° for eye position and to 10° per second for velocity. We have previously noted that no significant differences in PV existed between adduction and abduction saccades.[5] For every experimental situation in each subject, at least 100 measurements of PV at various amplitudes were obtained with the exception of post-rotary nystagmus where there were fewer measurements. We determined the mean peak velocity ($\overline{PV}$) for the entire group under all experimental situations at the various amplitudes.

Results. The $\overline{PV}$ of both voluntary saccades and fast phases of the different types of nystagmus in an illuminated environment is shown in Fig. 1. Statistical analysis using t-tests indicated no significant differences at any amplitude between the $\overline{PV}$ of voluntary saccades and nystagmus fast phases. All FEM showed a monotonically increasing relationship of $\overline{PV}$ and fell within the 95 per cent confidence limits for voluntary saccades in the normal population.[5]

Voluntary saccades greater than 4° in darkness were slower than those of the same amplitudes between visible refixation targets (Fig. 2). Similarly, the fast phases of caloric nystagmus in the dark were slower than in a lighted room (Fig. 3). Rotational tests in the dark provided insufficient data to define a significant difference but appeared generally slower, similar to saccades and caloric-induced fast phases.

There was considerable intra- and inter-subject variability for each type of FEM but each subject followed a pattern similar to the entire group with significant differences between conditions of illuminated environment and darkness. The standard deviations for each of the light-dark comparison groups are shown in Figs. 2 and 3.

Discussion. Ueda and Suzuki[8] conducted a pre-

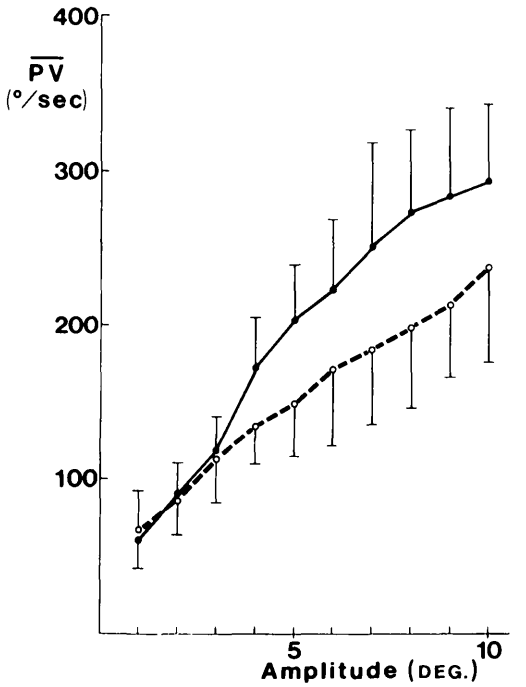

Fig. 2. Mean peak velocity ($\overline{PV}$)—amplitude relationships for FEM in light (●——●) and in darkness (○ - - - ○).

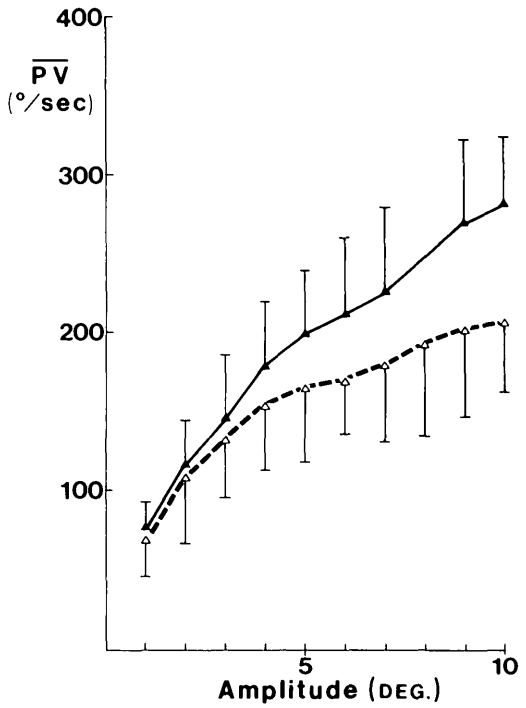

Fig. 3. Mean peak velocity ($\overline{PV}$)—amplitude relationships for fast phases of caloric-induced nystagmus in light (▲——▲) and in darkness (△ - - - △).

liminary study of the velocities of voluntary saccades and nystagmus fast phases in humans and concluded that they were similar. A detailed investigation in the monkey by Ron, Robinson, and Skavenski[9] showed that refixation saccades and rotational nystagmus fast phases had similar amplitude-duration relationships, although the latter were slightly faster. These same investigators found the fast phases of caloric-induced nystagmus slower than those obtained by rotation, chemical, or electrical stimulation of the vestibular system. Dichgans, Nauck, and Wolpert[10] reported that the fast phases of OKN were slightly slower than voluntary saccades in four human subjects but significantly slower only with amplitudes greater than 20° and in a leftward direction. Voluntary saccades were previously noted to be slower in darkness in both monkey[9] and man.[7] Rotational nystagmus fast phases in monkey are slower in darkness[9] but, although it was assumed that fast phases of both rotational and caloric-induced nystagmus in man were slower in darkness,[10] actual data were not presented.

Our findings of overlapping velocity-amplitude relationships for voluntary saccades and the fast phases of caloric, post-rotary, and OKN support the presumption that the identical brainstem unit activity responsible for the generation of all types of FEM in monkey[2, 9] occurs in humans as well.

We did not find the depression of caloric-induced fast phase velocities that Ron, Robinson, and Skavenski[9] noted in monkeys but this may be a function of the considerable amplitude disparities in the two studies. The monkeys had large amplitude caloric nystagmus, sometimes up to 50°, whereas in man the nystagmus did not exceed 10°. In addition to confirming that voluntary saccades are slow in darkness, we demonstrated that caloric-induced and probably rotational fast phases are also slowed.

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Key words: eye movements, fast eye movement, saccadic eye movements, saccades, nystagmus, nystagmus fast phases, caloric nystagmus, rotational nystagmus, optokinetic nystagmus, velocity-amplitude characteristics, eye movement recording, eye movement velocity.

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A directional impairment of eye movement control in strabismus amblyopia.

CLIFTON SCHOR.

Saccadic and pursuit tracking movements were elicited to determine the ability of the amblyopic eye to sense and respond to position and motion of the retinal image. Amblyopic eyes were found to initiate saccades as rapidly as normal eyes (200 to 300 msec.), however, the amblyopic eye's saccades were reduced in amplitude, highly variable, and required refinement by subsequent saccades, particularly in response to nasalward displacements of the retinal image. Pursuit responses of amblyopic eyes to both constant and sinusoidal velocity targets contained brief periods of abnormally slow following movements interrupted by position-corrective saccades. As with the saccadic response, the amblyopic eye's pursuit movements were more accurate for temporal than for nasal retinal image motion. Abnormal saccadic and pursuit eye movements in amblyopia result from reduced monocular position and velocity sensitivity probably associated with binocular suppression scotomas normally found in amblyopia.

There is strong evidence that large and unsteady movements of amblyopic eyes during attempted steady monocular fixation result from a region of reduced position sensitivity extending from the fovea of the amblyopic eye onto the nasal hemiretina.[1] Fixation errors containing prominant nasalward drifts and abnormally large saccades appear to be strategies adopted by the amblyopic eye to compensate for the region of reduced sensitivity. Nasalward drifts accompanied by frequent nasalward saccades lead to detectable position errors. In this manner the eye's position is sensed such that corrective temporalward saccades may be executed.

The current investigation examined the influence of the proposed region of reduced sensitivity on saccadic and pursuit tracking movements of amblyopic eyes. Previous studies have shown that tracking responses of amblyopic eyes to step changes of position or pendular motion of test targets are unsteady and irregular.[2] The amplitude and frequency of the unsteady eye movements are directly related to the degree of eccentric fixation and reduction of visual acuity of the amblyopic eye. This report demonstrates that tracking movements of amblyopic eyes are particularly abnormal when responding to targets imaged onto the nasal hemiretina. These results provide additional support for the presence of an asymmetric region of reduced sensitivity above the fovea of the amblyopic eye for both position and velocity of the retinal image.

Methods. Saccadic and pursuit tracking movements were recorded using a pair of infrared-sensitive diodes (LS 400 Texas inst.)[3] which were positioned before the subject's eye in a spectacle frame. Horizontal components of eye movements were sensed over a linear range from 15 arc minutes to 10 degrees, and recorded by a dual channel DC strip chart recorder. Monocular tracking responses to a small 3 arc minute spot moving in the horizontal meridian were recorded during a sixty-second period for the purpose of comparing eye position and movement control in normal and amblyopic eyes. Position control was examined by instructing subjects to track a slow (0.25 Hz.) or moderately fast (0.50 Hz.) square wave movement (6 degrees, peak to peak). Movement control was examined by in-