

# Vertical Optokinetic Nystagmus and Saccades in Normal Human Subjects

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**PURPOSE.** Optokinetic stimulation induces nystagmus that can be used to test the saccadic and visual-tracking systems in some patients with voluntary gaze palsies. The purpose of this study was to characterize vertical optokinetic nystagmus (OKN) in normal human subjects, comparing the dynamic properties of the quick phases with voluntary saccades of similar size and measuring the slow-phase responses to visual stimuli with a range of spatial and temporal frequencies.

**METHODS.** Vertical OKN and saccades were recorded in 10 healthy adult subjects (age range, 24–54 years) using the magnetic search coil technique. The optokinetic (OK) stimulus subtended 72° horizontally and 60° vertically, consisted of black-and-white stripes with a spatial frequency of 0.04, 0.08, or 0.16 cyc/deg, and moved vertically at 10 to 50 deg/s. Vertical and horizontal saccades to visual targets separated by 1° to 10° were also elicited.

**RESULTS.** Over 95% of quick phases were less than 10° in amplitude; voluntary saccades of this amplitude range were slightly faster than quick phases of similar size. The amplitude-peak velocity relationships and amplitude-duration relationships of upward and downward fast movements (saccades or quick phases) were similar. Most vertical slow-phase OK responses showed greater gain for upward stimulus motion. OK gain decreased with increasing stimulus speed and increased spatial frequency, so that there was a general decrease in slow-phase velocity gain with increasing temporal frequency.

**CONCLUSIONS.** In this study, the best OK responses were obtained using stripes with lower spatial frequencies and lower stripe speeds (0.4 cyc/deg at 10 deg/s). The dynamic properties of vertical quick phases of nystagmus are similar enough to those of voluntary saccades for OK stimulation to be used as a clinical test of the vertical saccadic system in individuals with voluntary gaze palsy. (*Invest Ophthalmol Vis Sci.* 2003;44:3833–3841) DOI:10.1167/iovs.03-0066

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Supported by the Iris Fund and Help a Child to See; Office of Research and Development, Medical Research Service, Department of Veterans Affairs; National Eye Institute Grant EY06717; and the Evenor Armington Fund.

Submitted for publication January 22, 2003; revised March 3 and April 9, 2003; accepted April 10, 2003.

Disclosure: **S. Garbutt**, None; **Y. Han**, None; **A.N. Kumar**, None; **M. Harwood**, None; **C.M. Harris**, None; **R.J. Leigh**, None

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During natural behavior, optokinetic nystagmus (OKN) is induced during self-rotation, when it supplements the vestibulo-ocular responses so that images are held fairly steadily on the retina and vision of the environment remains clear.<sup>1</sup> In clinical practice, OKN is a convenient way to test smooth visual tracking and resetting quick phases, which are generated by the saccadic system. For example, in children and patients with neurologic disorders who cannot cooperate with testing of voluntary eye movements, OKN can often be induced, especially using a moving stimulus that fills most of the visual field. Although there is a large body of knowledge concerning OKN in the horizontal plane, less is known about the normal vertical response, partly because of the technical difficulties in making reliable measurements of vertical eye movements. Nonetheless, a number of neurologic disorders—for example, Niemann-Pick disease type C in children and progressive supranuclear palsy in adults—cause selective defects in voluntary vertical gaze (for a reviews, see Refs. 2, 3). Testing vertical OKN in such patients may provide useful information, even in individuals who cannot easily cooperate with standard tests of vertical eye movements.

The magnetic search coil allows for accurate recording of vertical eye movements without distortion by concomitant lid movements. Several studies have delineated the range of dynamic properties of vertical saccades in normal subjects.<sup>4–11</sup> In contrast, there is little or no reliable information that compares the dynamic properties of vertical quick phases and saccades. Moreover, there is no agreement concerning vertical OKN slow-phase properties in normal humans. Some investigators have reported better slow-phase responses to upward than to downward stimulus movement<sup>12–21</sup> whereas other laboratories have reported the converse<sup>22–24</sup> or, depending on the stimulus speed, idiosyncratic differences in the directional asymmetry without a significant group effect.<sup>22,24–31</sup>

The goals of this study were to apply reliable methodology in 10 healthy human subjects to determine whether quick phases induced by vertical OK stimuli show similar dynamic characteristics to voluntary vertical saccades and to determine the slow-phase OK responses to a range of vertical OK stimuli to identify optimal speed and spatial frequency of stripe stimuli (which are commonly used in clinical practice).

## METHODS

### Subjects and Recording Methods

Ten healthy adult subjects were recorded (five women; age range, 24–54 years, median 31). None had any known neurologic or visual defects other than refractive anomalies. No subjects wore spectacle correction during the experiments. In addition, to demonstrate the potential clinical applications of our present study, we investigated a 74-year-old woman with impaired ability to make voluntary vertical saccades because of progressive supranuclear palsy (PSP) and, as a control, a 79-year old man with Parkinson’s disease (PD) who was able to make voluntary vertical saccades. All subjects and patients gave informed, written consent, in accordance with the Declaration of Helsinki and our institutional review board.

We measured horizontal and vertical movements using the magnetic search coil technique, with 6-foot field coils that used a rotating magnetic field in the horizontal plane and an alternating magnetic field in the vertical plane.<sup>32</sup> Search coils were worn binocularly in five subjects and monocularly in five. Of the five subjects who wore a search coil on one eye, two who normally wore corrective contact lenses continued to wear them on the nonrecorded eye. Of the five subjects who wore search coils on both eyes, two were emmetropes, and the refractive corrections in the others were 1.5, 2, and 3.5 D. Search coils were calibrated before each experimental session. The system was 98.5% linear over an operating range of  $\pm 20^\circ$ , the standard deviation of system noise was less than  $0.02^\circ$ , and crosstalk between vertical and horizontal channels was less than 2.5%.

Subjects sat in a stationary vestibular chair, with their heads maintained in an erect position by a cushioned support throughout the test period. Alertness was maintained by frequent verbal encouragement. The sequence of OKN or saccades testing was random in each subject. Each subject was tested during one session that lasted for approximately 20 minutes.

### Visual Stimuli

The OK stimulus was rear projected onto a semitranslucent tangent screen at a viewing distance of 1 m in an otherwise dark room. The stimulus subtended  $72^\circ$  horizontally and  $60^\circ$  vertically. Although this stimulus did not fill the visual field and did not produce circular vection (the illusion of self-rotation), it induced robust OKN in all our subjects. The OK stimuli were generated by a visual stimulus generator (VSG2/5; Cambridge Research Systems, Cambridge, UK) and projected by a video projector (Powerlite 9100i; Epson Seiko Corp., Nagano, Japan). The stimulus consisted of alternating black-and-white stripes, with luminance of 0.7 and 13.7  $\text{cd/m}^2$ , respectively, that moved upward or downward at one of three spatial frequencies: 0.04, 0.08, or 0.16  $\text{cyc/deg}$ . The direction and spatial frequency of the stimulus were randomized. Each sequence was viewed with both eyes open and the stimulus moved at 10, 20, 30, 40, and 50  $\text{deg/s}$  for periods of 20 seconds each. The screen was blank for 10 seconds between each sequence. Subjects were instructed to keep gazing into the center of the pattern, to try to maintain optimal clarity of the stripes, and not to follow any one stripe deliberately.

The stimulus for eliciting vertical saccades consisted of 13 black dots displayed on the screen. One dot was displayed in the center, one  $1^\circ$  above and below the center and thereafter one every  $2^\circ$  above and below, up to  $10^\circ$  eccentricity. To elicit voluntary vertical saccades, subjects were instructed to perform two patterns of refixations. First, they were asked to move their point of visual fixation from the center dot to the dot located at  $1^\circ$  in the upper field, back to the center dot, to the  $2^\circ$  dot, back to the center dot, and to successive eccentric dots until the  $10^\circ$  dot had been reached. In this pattern, up and down saccades were made entirely within the upper visual field. Second, refixations were made between the center dot and the dots in the lower field. Horizontal saccades were similarly elicited using the same stimulus as for vertical saccades, rotated through  $90^\circ$ .

### Data Analysis

To avoid aliasing, coil signals were passed through Krohn-Hite Butterworth filters (bandwidth, 0–150 Hz) before digitization at 500 Hz with 16-bit resolution. These digitized signals were then passed through an 80-point Remez finite impulse response filter (bandwidth 0–140 Hz), and differentiated to yield eye velocity.<sup>32</sup>

All measurements were checked interactively, and eye movements associated with blinks were rejected. We separately analyzed data from each eye in the five subjects who wore a coil in both eyes (group total of 15 data sets from 10 subjects). The goal of measuring two eyes in five subjects was to confirm that nystagmus was similar in the two eyes. A saccade or OKN quick phase (fast eye movement; FEM) was detected when the velocity was continuously above 10  $\text{deg/s}$  for at least five points. The peak velocity of each FEM was then determined.

FEM onset and offset were defined as the last points on either side of the peak velocity before which the velocity declined below 10  $\text{deg/s}$ . These points were used to calculate the amplitude and duration of the FEMs. We constructed logarithmic (base 10) plots of peak velocity against amplitude and performed linear regressions for saccades or quick phases for each data set from each eye to calculate the intercept and slope. The mean  $\pm$  SD  $R^2$  of the regression fits for the 10 subjects was  $0.90 \pm 0.07$ . We then performed paired comparisons of the values of intercept and slope for the group of 10 data sets, for saccades or quick phases, in each direction, using a paired *t*-test, or the Wilcoxon signed rank test if the distribution of data was not normal. As a further statistical test we also used a multivariate analysis of variance (MANOVA), taking the slope and intercept as the independent variables. Consistent results were obtained throughout our study with these two statistical methods, and the results presented are from the paired data comparisons. Statistical significance was assumed at a  $P = 0.05$  level throughout. We also compared responses from fellow eyes in the five subjects who wore two search coils.

Because the relationship between duration and amplitude of FEMs is nonlinear below  $4^\circ$  and many of our quick phases were smaller than this (see the Results section), we also constructed logarithmic plots of duration against amplitude and performed linear regressions for saccades or quick phases for each data set from each eye to calculate the intercept and slope. The mean  $\pm$  SD  $R^2$  of the regression fits for the 10 subjects was  $0.81 \pm 0.10$ . The statistical tests just described were used to determine whether there was a difference in the durations of vertical saccades and vertical quick phases.

We measured slow-phase velocity interactively by placing cursor marks at the beginning and end of each movement. The program then calculated mean eye velocity for each slope based on all the points between the two cursor marks. At each stimulus speed, the OKN gains were calculated by averaging (mean) over all the slow phases.

## RESULTS

### Quick Phases and Saccades

Of 16,604 quick phases of nystagmus analyzed in the 10 subjects, more than 95% were less than  $10^\circ$  in amplitude (median,  $2.1^\circ$ ). Accordingly, we compared vertical saccades and quick phases of OKN for amplitudes up to  $10^\circ$ . We performed an analysis of quick-phase amplitude in response to the different speeds and spatial frequencies of the stimuli used, but the differences were not consistent. Thus, the amplitude of the OK quick phases did not depend on the speed or spatial frequency of the stimulus.

The analyses of the relationships between amplitude, peak velocity, and duration of vertical quick phases and vertical saccades are summarized in Table 1 and for horizontal quick phases and horizontal saccades in Table 2. Representative data from one subject are plotted in Figure 1 and group amplitude-peak velocity and amplitude-duration results are summarized in Figure 2.

### Upward Versus Downward FEMs

For the group of 10 subjects, there were no significant differences in peak velocity or duration between upward or downward voluntary saccades of similar amplitude. Similarly, there were no significant differences in peak velocity or duration between upward or downward quick phases of similar amplitude.

### Centripetal Versus Centrifugal Vertical Saccades

In a further analysis, we compared saccades made in the upper visual field to those made in the lower field. Based on our regression analysis, upward saccades made in the upper visual field (centrifugal saccades) showed peak velocities and dura-

TABLE 1. The Main Sequence Parameters for Duration and for Peak Velocity for Vertical Saccades and Quick Phases

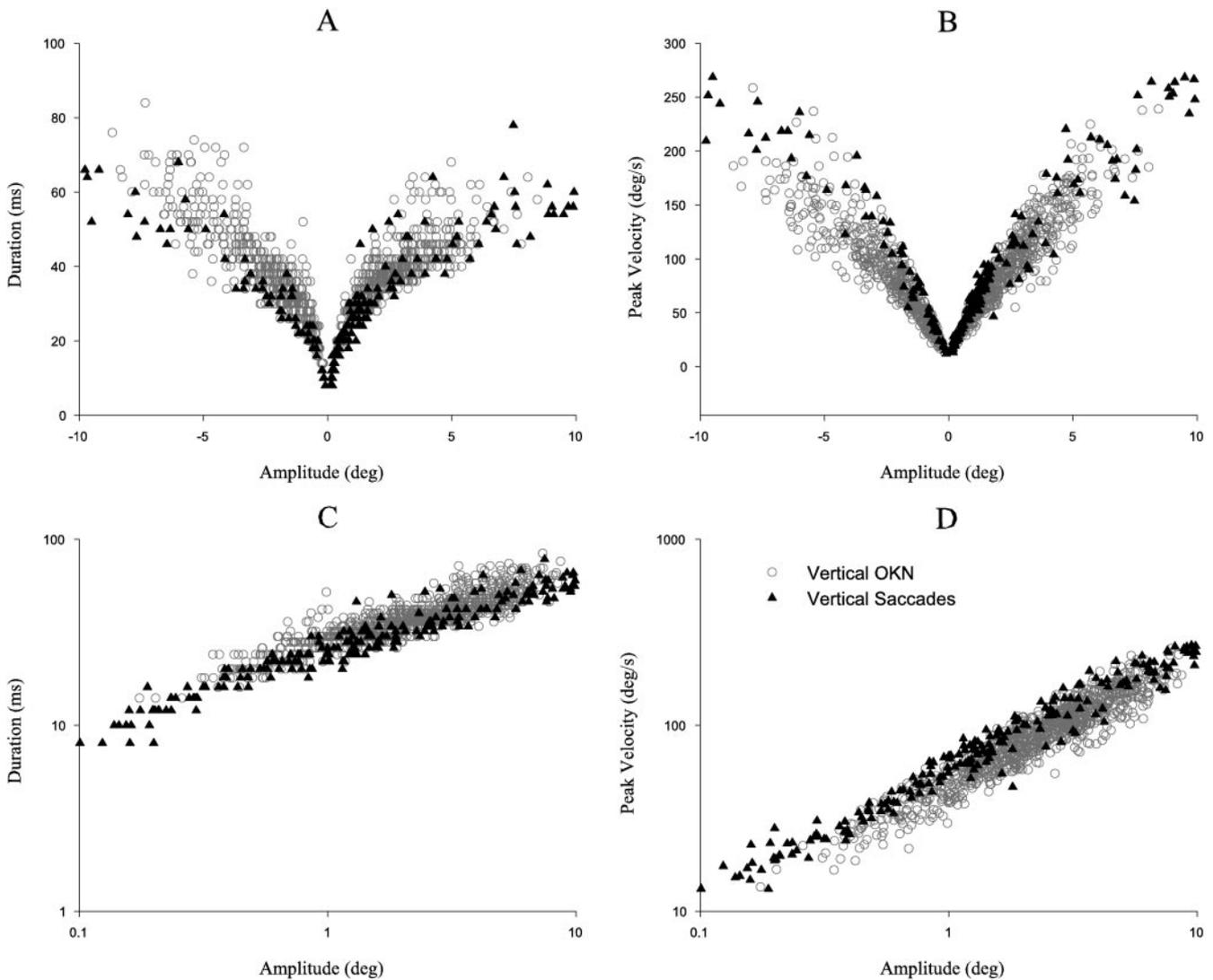
Subject/ Eye	Duration-Amplitude Relationship						Peak Velocity-Amplitude Relationship					
	Saccades			OKN Quick Phases			Saccades			OKN Quick Phases		
	Up	Down	Mean	Up	Down	Mean	Up	Down	Mean	Up	Down	Mean
1	3.1	24.6	3.3	24.6	2.3	31.6	4.3	58.9	4.2	58.9	5.0	41.7
2	2.8	25.1	3.3	27.5	3.6	25.7	4.7	57.5	3.7	52.5	3.4	52.5
3	2.7	25.1	2.6	24.0	2.2	28.2	4.6	57.5	5.0	60.3	5.0	50.1
4	3.0	28.2	3.0	30.9	2.6	29.5	4.6	51.3	4.8	46.8	4.9	44.7
5	3.0	24.6	2.5	22.4	3.2	30.2	4.4	60.3	5.1	67.6	4.3	49.0
6	2.9	26.9	2.8	25.1	2.8	26.3	4.2	56.2	4.4	57.5	3.9	45.7
7	2.7	24.0	2.6	25.7	2.4	30.2	4.9	63.1	4.5	56.2	4.7	49.0
8	2.7	23.4	3.2	22.4	3.0	25.1	4.5	60.3	3.6	66.1	4.0	55.0
9	2.8	22.9	2.6	21.9	2.4	25.7	4.1	64.6	4.4	69.2	4.6	56.2
10	2.5	24.6	3.1	26.3	2.8	28.8	4.8	56.2	4.3	55.0	4.4	45.7
Mean ± SD	2.8 ± 0.2	24.9 ± 1.6	2.9 ± 0.3	25.1 ± 2.7	2.7 ± 0.4	28.6 ± 2.3	4.5 ± 0.3	57.6 ± 3.8	4.4 ± 0.5	59.0 ± 7.1	4.4 ± 0.5	49.0 ± 4.7

The main sequence parameters for duration and for peak velocity for vertical saccades and vertical OKN quick phases of less than 10° amplitude. The slope (S) and intercept (I) for the duration-amplitude relation were obtained from a linear regression of the logged main sequence for duration, expressed in milliseconds, as in Figure 1C. The S and I values for the peak velocity-amplitude relation were obtained from a linear regression of the logged main sequence for peak velocity, as in Figure 1D. Unlogged values are shown. Pooled means ± SD are also shown. For those subjects in whom both eyes were recorded, data from the left eye arc presented, and it was this data that was used for analysis. RE, right eye; LE, Left eye.

TABLE 2. The Main Sequence Parameters for Duration and for Peak Velocity for Horizontal Saccades and Quick Phases

Subject/ Eye	Duration-Amplitude Relationship						Peak Velocity-Amplitude Relationship					
	Saccades			OKN Quick Phases			Saccades			OKN Quick Phases		
	Right	Left	Mean	Right	Left	Mean	Right	Left	Mean	Right	Left	Mean
1	2.6	22.9	2.6	16.6	2.9	22.9	5.0	66.1	4.3	89.1	3.8	64.6
2	2.7	26.3	2.5	25.1	2.6	22.4	4.6	56.2	4.6	58.9	3.5	70.8
3	3.6	19.5	3.2	22.4	2.7	24.6	3.1	72.4	3.3	66.1	3.2	64.6
4	2.7	21.4	2.3	19.5	2.0	23.4	5.3	70.8	5.3	75.9	5.5	58.9
5	2.7	19.5	2.6	19.5	2.4	22.9	4.7	74.1	4.6	75.9	5.1	63.1
6	2.8	20.9	2.8	22.4	2.6	24.6	4.5	70.8	4.3	66.1	3.8	58.9
7	2.9	20.0	2.1	28.2	2.6	21.4	3.5	89.1	4.6	72.4	3.9	74.1
8	2.8	20.0	2.8	19.1	2.8	25.1	4.1	72.4	3.8	75.9	3.8	55.0
9	2.5	21.9	2.2	20.4	2.2	24.0	5.0	67.6	5.5	72.4	6.0	61.7
10	2.6	19.5	2.6	20.0	2.5	26.9	4.8	72.4	4.8	72.4	4.9	52.5
Mean ± SD	2.7 ± 0.4	21.2 ± 2.1	2.6 ± 0.3	21.3 ± 3.3	2.5 ± 0.3	23.8 ± 1.6	4.4 ± 0.7	71.2 ± 8.2	4.5 ± 0.6	72.5 ± 8.0	4.3 ± 1.0	63.4 ± 6.6

The main sequence parameters for duration and for peak velocity for horizontal saccades and horizontal OKN quick phases of less than 10° amplitude. See Table 1 for an explanation of the data.



**FIGURE 1.** Representative vertical saccadic and OKN quick-phase main sequences for duration and peak velocity. These plots were derived from vertical saccades (▲) and vertical OKN quick phases (○) of less than  $10^\circ$  amplitude recorded from subject 3. (A) Scatterplot of the vertical saccadic and vertical OKN quick-phase main sequences for duration. Negative values represent eye movements downward. (B) Scatterplot of the vertical saccadic and vertical OKN quick-phase main sequences for peak velocity. Negative values represent eye movements downward. (C) Logarithmic plot of duration versus amplitude (upward and downward movements combined). (D) Logarithmic plot of peak velocity versus amplitude (upward and downward movements combined).

tions similar to those of upward saccades made in the lower visual field (centripetal saccades). However, downward saccades made in the lower visual field (centrifugal saccades) were faster than downward saccades made in the upper visual field (centripetal saccades), based on significant differences of the slopes of the regressions ( $P < 0.001$ ). Intercepts were not significantly different.

### Vertical Quick Phases Versus Vertical Saccades

A comparison of vertical voluntary saccades showed them to be consistently faster (greater peak velocity and smaller duration) than quick phases of similar size and direction (Figs. 1A, 1B). Statistical comparison of the linear regressions of the log curve-fits (see example in Figs. 1C and 1D) showed a significant difference in the intercept ( $P < 0.005$ ) but not in the slope.

### Vertical Versus Horizontal FEMs

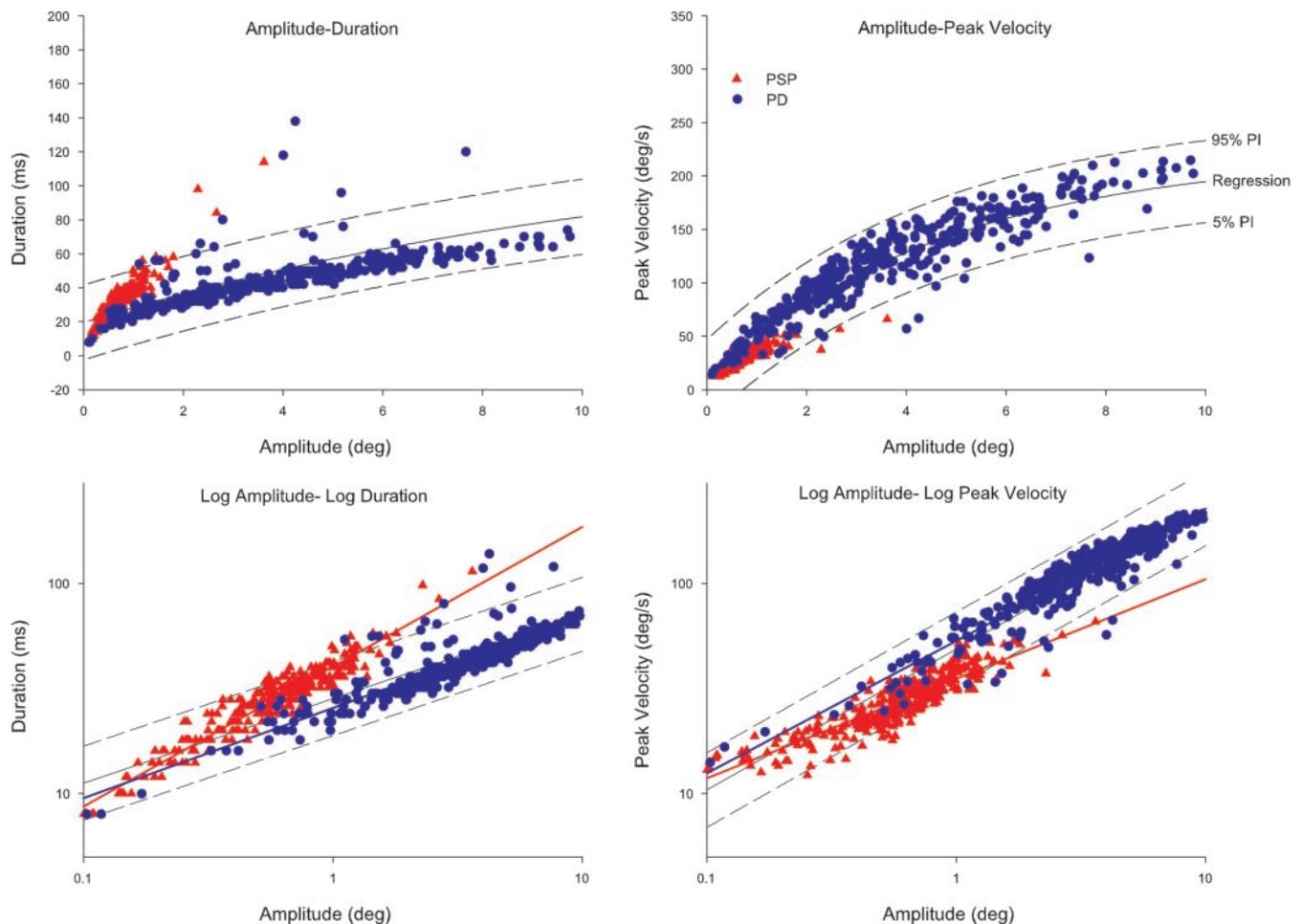
We also compared vertical saccades (Table 1) with horizontal saccades (Table 2) and found that they had a significantly

different duration and peak velocity ( $P < 0.01$ ). Vertical saccades were slower than horizontal saccades, with longer durations and lower peak velocities. Similarly, there were significant differences in peak velocity and duration between vertical and horizontal quick phases (Tables 1, 2).

### OKN Slow-Phase Velocity

In most of the subjects, vertical OKN slow-phase gain was either symmetrical in response to upward or downward stimulus motion or, more commonly, there was an asymmetry, with the response to downward motion having a lower gain. Only occasionally was the response to downward motion greater than the response to upward motion (Fig. 3). Overall, the gain of upward OKN was greater than that of downward OKN by an average of  $0.09 \pm 0.11$  (SD).

There was a decrease in slow-phase velocity gain with increasing spatial frequency and increasing stimulus velocity, so that there was a general decrease in slow-phase velocity gain with increasing temporal frequency (Table 3).



**FIGURE 2.** Plots showing regression, 5% and 95% prediction intervals for all quick-phase data from the 10 normal subjects. Also shown are quick phases from a patient with PSP, who had difficulty making vertical saccades, and a patient with PD, who could make normal vertical saccades. Note that although most data points of the patients with PSP or PD lay within the 95% bounds, on the log-log plots (*bottom* panels) the regression of the data of the patient with PSP (for duration slope = 4.62, intercept = 40.18; for peak velocity slope = 2.95, intercept = 35.48) differed significantly from the normal subjects' ( $P < 0.05$ ), but the regression of the data of the patient with PD (for duration slope = 2.68, intercept = 25.58; for peak velocity slope = 4.27, intercept = 53.70) did not.

### Comparison of Responses from Fellow Eyes

Paired comparison of the quick-phase and slow-phase variables presented in these results showed no significant differences between the two eyes of any of the five subjects who wore a search coil on both eyes.

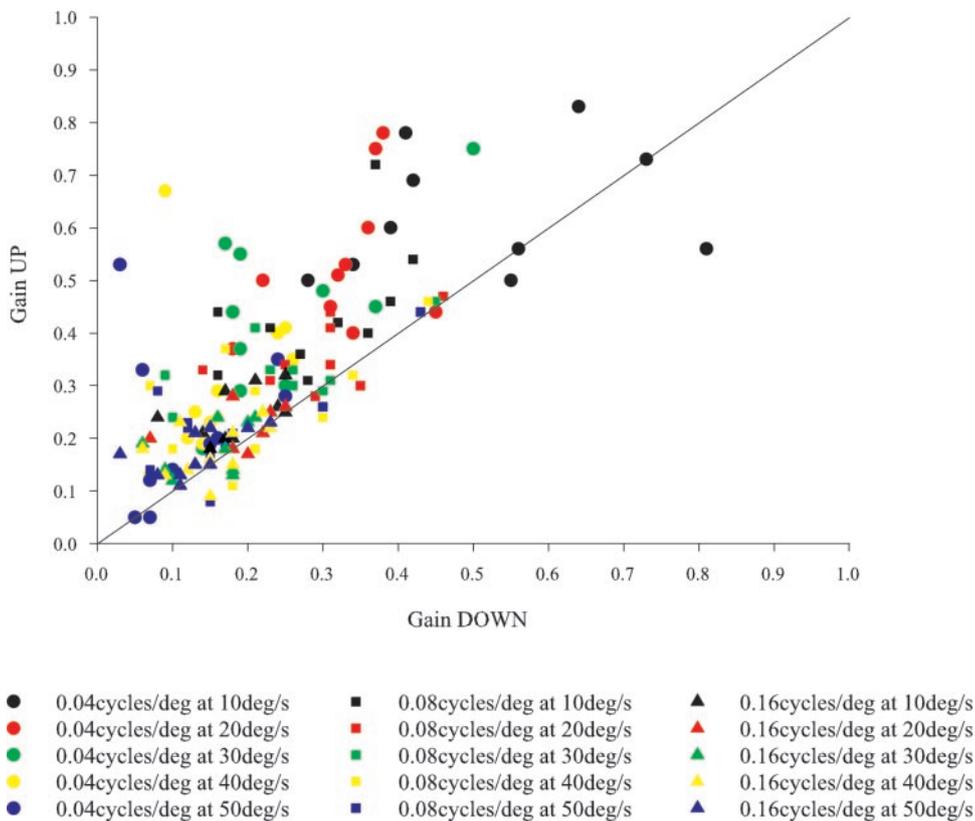
### DISCUSSION

The main findings of this study are that, in general, vertical quick phases shared similar dynamic properties with saccades of similar size and that the slow-phase component of vertical OKN was optimally elicited with low stimulus speeds and low spatial frequencies (low temporal frequencies). We discuss the implications of these findings as follows: (1) vertical saccades compared with vertical OKN quick phases; (2) vertical saccades compared with horizontal saccades; (3) vertical OKN slow-phase gain compared with prior studies; and (4) the clinical implications of our findings.

### Comparison of Vertical Saccades with Vertical OKN Quick Phases

For amplitudes up to  $10^\circ$ , vertical saccades and vertical OKN quick phases had similarly shaped main sequences for duration

and for peak velocity (Fig. 1). However, vertical saccades were slightly faster than vertical OKN quick phases, having shorter durations and reaching higher peak velocities. We considered whether these differences might be an artifact of our method of analysis, which used a velocity criteria of 10 deg/s. First, we compared results using thresholds of 10 and 20 deg/s on the quick-phase data set from one subject. Results differed by 6% for the slope and less than 1% for the intercept (the parameter which identified differences between quick phases and saccades). Second, we used a simple additive model in which we added slow-phase drift of 10 deg/s to recorded saccades. Thus, whereas a voluntary upward saccade started from a velocity of 0 deg/s, an upward quick phase (during downward OK stimulus motion) started from a velocity of  $-10$  deg/s. This model predicts that it takes longer for a quick phase to cross the velocity threshold than a saccade and that the quick phases drop back below the threshold at an earlier point than the saccade. The result is that quick phases are measured as smaller, slower, and shorter in duration than similar-sized saccades. Thus, a simple additive model predicts that measurements of amplitude, duration, and peak velocity will all be different from measurements of similar-sized saccades, if a velocity threshold method is used. For this reason, it is difficult to decide whether quick phases are slower and longer than



**FIGURE 3.** Upward versus downward OKN gain. Upward slow-phase velocity gain was plotted against downward slow-phase velocity gain for each subject at each stimulus speed (represented by the five different colors) and each spatial frequency (represented by the three different shaped symbols). *Dotted line:* upward gain was equal to downward gain. Points above the *dotted line* indicate that upward gain was greater than downward gain. Points below the *dotted line* indicate that the reverse was true.

similar-sized saccades based on main-sequence relationships. However, an independent factor arguing against the influence of slow-phase velocity on our measurements of quick phases is that the differences between saccades and quick phases were greater for upward rapid movements. We found that OKN slow-phase gain was consistently greater with upward stimulus motion, and this would be expected mainly to affect downward quick phases, if slow-phase velocity was the cause of the different dynamic properties of saccades and quick phases. Thus, on balance, we suspect that our finding of vertical quick phases being slower than voluntary vertical saccades reflects biological rather than methodological factors. FEMs are known to be affected by a variety of experimental conditions and, for example, it has been demonstrated that visually triggered saccades are faster than voluntary saccades.<sup>33</sup> Similarly, quick phases of OKN, which are more reflexive, may be slower than visually triggered saccades. Further work is needed to clarify this issue.

Although we have shown that there are subtle differences in the speed of vertical FEMs depending on how they are elicited, clinical and neurophysiological studies indicate that both types of movement are generated in the midbrain, by burst neurons in the rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF), which project to ocular motoneurons.<sup>34,35</sup> Bilateral chemical lesions of the riMLF in monkey abolish all vertical FEMs.<sup>36</sup> In humans also, bilateral infarctions in the region of the riMLF lead to a loss of vertical saccades and vertical OK quick phases.<sup>3,37</sup> In progressive disorders that affect the rostral midbrain, such as Niemann-Pick disease type C, the first oculomotor abnormality is a selective slowing of vertical saccades<sup>11</sup> and then loss of vertical saccades, together with an absence of OKN quick phases in the vertical plane.<sup>38,39</sup> We will discuss the clinical implications of these findings later.

### Comparison of Vertical and Horizontal Saccades

We found that there were no statistical differences between the peak velocity or duration of upward and downward saccades. In three other studies investigators using the search coil method also found that upward and downward saccades were similar for amplitudes of up to 20°.<sup>4,7,8</sup>

The dynamics of vertical saccades, as measured by the main sequences for duration and peak velocity, have been variously reported to be the same or slower than those of horizontal saccades.<sup>7-9</sup> We found that the main sequences for duration and peak velocity of vertical and horizontal saccades have the same basic shape. For both horizontal and vertical saccades above amplitudes of 4°, duration increased linearly with amplitude. For both directions, peak velocity increased exponentially with amplitude. However, although the main sequences of horizontal and vertical saccades had similar shapes, vertical saccades were slower than horizontal ones.

A study of a subject's saccades in the four main directions (left, right, up, down) often reveals idiosyncratic directional anisotropies.<sup>40</sup> It is established that horizontal centripetal saccades are generally faster than horizontal centrifugal saccades.<sup>41-46</sup> However, it is not clearly established whether there are similar consistent differences between centripetal and centrifugal vertical saccades. Over the range of amplitudes that we elicited (up to 10°) we found that upward centrifugal saccades showed peak velocities and durations similar to those of upward centripetal saccades. However, downward centrifugal saccades were faster than downward centripetal saccades.

### Vertical OKN Slow-Phase Gain

We found that the two eyes are yoked during vertical OKN, but there was a clear up-down asymmetry. OKN in response to upward stimulus motion had a higher gain than OKN in response to downward stimulus motion. This asymmetry was

TABLE 3. Vertical Slow-Phase Velocity Gain Dependence on Temporal Frequency of the Stimulus

	0.4	0.8	1.2	1.6	2.0	2.4	3.2	4.0	4.8	6.4	8.0
Up gain	0.66 ± 0.12	0.50 ± 0.13	0.43 ± 0.13	0.31 ± 0.10	0.23 ± 0.13	0.32 ± 0.06	0.24 ± 0.08	0.22 ± 0.09	0.20 ± 0.04	0.19 ± 0.05	0.19 ± 0.04
Down gain	0.57 ± 0.14	0.34 ± 0.05	0.26 ± 0.10	0.23 ± 0.13	0.12 ± 0.07	0.29 ± 0.06	0.22 ± 0.07	0.20 ± 0.10	0.18 ± 0.04	0.17 ± 0.04	0.15 ± 0.04

Temporal frequency (Hz) of stimuli are shown in bold; data are gain ± SD.

found at all the stimulus speeds that we used (10–50 deg/s). Similarly van den Berg and Collewijn,<sup>16</sup> using the magnetic search coil technique, found that downward OKN had a gain that was lower than upward OKN by approximately 0.15. This asymmetry was also described by Takahashi et al.<sup>12</sup> and Ogino et al.<sup>20</sup> A similar up-down asymmetry has been found in other frontal-eyed animals (monkey<sup>47–52</sup> and cat<sup>26,53–56</sup>).

It appears, therefore, that in frontal-eyed animals such as humans, there is an asymmetry of vertical OKN, with a greater response being elicited by an upward-moving stimulus. During forward movement in frontal-eyed animals, the predominant asymmetries in flow fields are in the vertical domain. Thus, when a frontal-eyed animal moves forward while looking straight ahead, it is necessary to prevent the OK reflex from rotating the eyes downward in response to optic flow of the highly textured ground plane. Stereopsis cannot stabilize the centrifugal optic flow pattern; therefore, it has been suggested<sup>17</sup> that in such animals an upward preponderance of OKN develops, to dampen the influence of the prominent downward optic flow that is present in the lower visual field (i.e., the part of the field that contains the greater richness of visual information). Thus, the lower sensitivity of the OKN system to downward motion in frontal-eyed animals most likely compensates in part for the visual dominance of the lower field<sup>57</sup> and allows for better stabilization of the visual field during forward locomotion.

Conversely, in the rabbit, which has eyes that are low and lateral, there is little difference between upward and downward OKN, although nonhorizontal responses are limited to very low velocities. During forward movement in lateral-eyed animals visual flow fields show a marked asymmetry of temporal-directed as opposed to nasal-directed optic flow.<sup>58</sup> Thus, the largest asymmetries in optic flow, and in OKN, in such animals are almost totally in the horizontal plane.

### Clinical Implications

It should be noted that the stimulus we used did not induce circular vection, and we did not study OK after-nystagmus, which is a measure of “velocity storage” in the optokinetic-vestibular system.<sup>47</sup> Responses in our subjects were therefore driven by visual motion stimuli that activate both smooth pursuit and OK systems.<sup>2</sup> However, the goal of our study was not to investigate the OK system per se, which has been the focus of several prior studies, but rather to define the features of OKN that would be useful in clinical testing of patients who cannot respond to small visual stimuli or make voluntary saccades.

To illustrate the potential application of eliciting quick phases with an OK stimulus in patients who have impaired ability to initiate voluntary saccades, we studied a patient with PSP. This disease causes slowing and eventually loss of all vertical saccades.<sup>59</sup> Our patient was able to make small and slow voluntary vertical saccades, but with difficulty. In Figure 2, we have plotted quick-phase data from this patient and compared the results with prediction intervals of normal subjects derived from the present study. As a control, we also plotted OK quick-phase data from an age-matched patient with PD who did not have a defect of voluntary vertical saccades. It is evident that the patient with PSP has smaller, slower, and longer-duration quick phases than the control populations. These differences are most evident on the log-scale plots, where both slope and intercept differ significantly from the fitted parameters for our normal subjects (Table 1). The patient with PD was similar to control subjects. These preliminary findings indicate that OK stimulation could be used as a clinical test of the vertical saccadic system in individuals who are unable to cooperate with saccadic testing, and is the subject of an ongoing study.

## SUMMARY

In this study, the optimal stimulus to elicit OKN (highest gain of slow phases) was black-and-white stripes with lower spatial frequencies and lower stripe speeds (0.4 cyc/deg at 10 deg/sec). Although we did not specifically test smaller stimuli, a large moving visual display is known to be superior to a handheld drum. Also, our experience is that children, in particular, respond better to moving lines than random-dot patterns. The stimuli that we used in these experiments induced responses that can be used to test both visual tracking abilities and the saccadic system by quick phases that are induced.

## Acknowledgments

The authors thank David Riley for referring one of the patients.

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