MEASUREMENT OF OPTOKINETIC NYSTAGMUS FOR OTONEUROLOGICAL DIAGNOSIS

SHARON M. ABEL, PhD HUGH O. BARBER, MD, FRCS(C)

TORONTO, ONTARIO, CANADA

Optokinetic nystagmus was recorded and measured in 101 subjects comprising six diagnostic categories: 1) normal, screened for otologic disease, 2) chronic unilateral labyrinthectomy, 3) unilateral Menière's disease, 4) neurologically confirmed focal brainstem lesion, 5) brainstem-cerebellar syndrome, and 6) focal unilateral supratentorial lesion. For the OKN test, each subject looked at a translucent screen onto which a field of parallel black and white bars was back-projected. The array of bars could be projected vertically or horizontally to allow for study of nystagmus beating right and left or up and down. The speed of movement of the bars varied over a range from 20 to 140°/sec of visual angle, in each axis for both directions.

An analysis of the slow phase velocity of OKN indicated that patients with brainstem disease produced significantly lower eye speeds than did normal subjects or patients with chronic peripheral vestibular disease. The latter groups could not be distinguished. The responses of patients with cortical lesions fell midway between these two extremes and were significantly different from those of the brainstem group. Directional preponderance of nystagmus proved to be significantly related to the side of lesion for both the labyrinthine and cortical groups. However, the absolute value of the difference in slow phase velocity for nystagmus beating toward or away from the side of lesion was no greater than the difference between right and left-beating nystagmus in normal subjects. While the results provide statistical confirmation for the findings of earlier investigations, it is noted that for purposes of clinical diagnosis, the test is of value only in the context of the otoneurological test battery. Distribution of results for individuals in the various groups overlap considerably. The designation of a numerical cutoff for differential diagnosis leads to error rates far in excess of what may be confidently attributed to chance.

Observation of optokinetic nystagmus (OKN) has been included in both neuro-opthalmologic and otoneurologic examinations for the past 50 years.[1-3] The response has been used to assess higher cortical function, as well as the integrity of a variety of systems, including the peripheral and central oculomotor and vestibular pathways; abnormalities have been reported in the presence of lesions throughout the brain.[4]

The examination is easily performed. One method is to use a small drum, about 30.5 cm in diameter, with alternating black and white stripes, which is held about 46 cm in front of the patient's eyes and slowly rotated. In place of the drum, many clinicians use a tape consisting of a series of colored patches sewn on a strip of white cloth. The strip is moved slowly to the right or left, up or down. The patient is instructed to gaze straight ahead at the stripes (or visual targets) without deliberate fixation. Typically, if the targets move continuously from left to right, the eyes will alternately move slowly to the right and quickly return to the midline position. The speed of the slow phase is generally related to the speed of movement of the targets, increasing to about 50°/sec for a target speed of 80°, and then slowly decreasing as adjacent targets begin to fuse.[5-9]

The eye movement may be evaluated using qualitative description. For example, Smith[10] rates the response on a categorical scale from brisk to nil. Alternately one may use the techniques of electronystagmography.[8,9,11] The former method is entirely subjective and relies wholly on the impression of the examiner. The latter method gives an objective analogue representation of the eye movements on a polygraph recorder. The response appears as a triangular wave for each cycle of nystagmus (slow plus quick phase). The slope of the slow component gives the velocity of movement of the eyes in relation to the movement of the targets. One may also calculate the frequency of the response, ie, the number of beats (quick phases) per second, and the amplitude of response, ie, the maximum excursion of the eyes from the midline position.

SYNOPSIS OF THEORY OF CLINICAL FINDINGS

Several proposals have been made to describe the neurologic pathways subserving optokinetic nystagmus. The most widely popularized views are those of Cords[3] and Ling and Gay.[12]

Cords' hypothesis,[3] published in 1926, has been well described by Carmichael et al.[13] Briefly, the theory states that for targets moving from left to right, impulses from the right halves of the two retinae are projected to an optomotor center in the right peristriate cortex. Way stations include the right external geniculate body, optic radiation and visual cortex. For the efferent leg of the reflex, fibers from the peristriate area join the posterior part of the optic radiation and move forward, leaving the optic radiation at its anterior third to join the cerebral peduncle. From here fibers cross the midline to the posterior longitudinal bundle on the opposite side and go to the center for conjugate gaze in the pons.

From the Departments of Otolaryngology at Sunnybrook Medical Centre and the University of Toronto. This research was supported by grant No. MA-5209 from the Medical Research Council of Canada.

Cords' system predicts that a lesion anywhere along the path from the optomotor center in the cortex to the pontine gaze center will result in the abolition of OKN beating left. If the lesion occurs in that part of the path associated with optic radiation, then the added feature of homonymous hemianopia will appear. This syndrome of unilateral OKN deficit together with field blindness should be evident primarily in cases of deep parietal lesions. On the other hand, lesions involving the optic tracts, lateral geniculate body, temporal or occipital lobes might produce hemianopia but OKN should be brisk bilaterally.

Evidence in support of Cords' hypothesis has been given by Smith[10] and Cogan and Loeb.[14] Smith describes the findings of Kestenbaum[15] for a series of 59 cases of homonymous hemianopia. The data, based on visual inspection of the eyes by the examiner, indicate that in 28 instances of a positive optokinetic sign (ie, clear asymmetry in horizontal OKN) 10 were associated with lesions close to and 17 within the parietal region. For 24 instances of negative optokinetic sign, (ie, brisk response bilaterally) there were 10 patients with lesions distant from, and 5 with lesions close to the parietal region.

Smith's own observation of OKN in 100 patients with homonymous hemianopia are also reported in his monograph. Again the response was elicited using a strip of cloth and described on a four-point rating scale. An asymmetry in response, right-beating versus left-beating, was observed in 28 of 33 cases of parietal lesion. In the presence of a temporal lobe lesion, either proven or judged clinically, 19 of 24 patients showed negative OKN signs. For 39 occipital lobe lesions the OKN sign was negative in 31 instances, positive in 7, and absent in 1. In the presence of an occipital field defect, a negative OKN sign usually signified a vascular lesion, whereas a positive OKN sign was associated with a mass lesion (Cogan's Rule). Details of this research and autopsy study are given in Smith[16] and Smith and Cogan.[17,18]

Cords' predictions appear to be supported. Smith emphasizes that the hypothesis applies specifically to cerebral lesions and not to brainstem disease. He notes that in cases of brainstem involvement there may be a generalized depression or total absence of OKN. The latter finding may also be due to sedation or low vision.

Evidence against Cords' hypothesis has also been reported. Davidoff et al[19] studied OKN for a variety of cerebral lesions in a series of 37 patients. Each patient was placed for testing inside a rotating drum 91 cm in diameter and 61 cm in height. Normal OKN was defined as regular, rhythmical, symmetrical, well-sustained nystagmus with readily identifiable quick and slow components for both directions of the drum. An attempt was made to correlate the site of major brain damage and defects in horizontal OKN, although as the authors point out, strict anatomic correlation is often precluded by the multiplicity of lesions and extent of involvement. Other parts of the brain may be implicated by the pathological process.

The results showed that of the patients with abnormal OKN, 13 had tumors limited to cortex and underlying white matter of cerebral hemisphere. The OKN was "defective" when the drum was rotated toward the side of the lesion. Three patients had predominantly frontal lobe lesions, two temporal and four parieto-occipital lesions. The rest had lesions involving more than one lobe. Normal responses were found in patients with extensive lesions in the parietal lobe, hypothalamus, the lateral and anterior parts of the brainstem, and in patients with unilateral, bilateral, or diffuse lesions. Thus, the conclusion reached by the authors was that no correlation was possible between any specific type of optokinetic dysfunction and pathology involving any specific anatomic area. However, the claim was made that the test had use in lesion lateralization. The authors stated that, "In general, the more massive the disturbance in motor, somato-sensory and visual function, the more probable a defect in optokinetic nystagmus would be elicited."[19] This was especially true if a decrease in the state of alertness was also present. The results showed that normal OKN bilaterally was observed in cases of severe visual field deficit. Patients with gaze palsy showed defective OKN when the direction of defective gaze movement and direction of defective optokinetic response coincided.

A second major theory, not widely popularized, is that there are two centers for OKN, one in the frontal lobe and the second in the occipital lobe.[20] Recently, Ling and Gay[12] have attempted an expansion of this view. According to these investigators, any proposal for an OKN pathway must take into account the following facts:

1. The afferent limb of OKN is the same as that for visual afferents. Only one occipital lobe is required; thus, unilateral occipital lesions do not affect OKN.

2. The slow phase of OKN is mediated through the optomotor field of the occipital lobe. The mechanism is the same as that for ocular pursuit; the efferent path leads directly from the occipital lobe to the brainstem.

3. The fast phase depends on frontal lobe activity. The assumption is made that the pathway from frontal lobe to brainstem nuclei is identical to that for the fast phase of vestibular nystagmus and voluntary gaze.

4. Most patients with asymmetric OKN due to cerebral lesions have involvement deep in the parietal lobe. The abnormality is seen as a loss of the fast phase to the side opposite the lesion.

These facts suggest the following mechanisms:

> "Afferent impulses for the optokinetic reflex travel the visual pathway to the occipital lobe. This initiates the slow phase of the reflex, causing the eyes to deviate conjugately to the side toward which the target is moving. The efferent impulses for the slow phase travel directly to the brainstem from the occipital lobe. At the completion of the slow phase, the frontal lobe on the side toward which the eyes are deviated initiates the fast corrective phase of the reflex. This frontal lobe is activated by impulses from both the ipsilateral, and by way of the corpus callosum, the contralateral occipital lobe. The impulses from the frontal lobes in optokinetic nystagmus travel to the brainstem in the same pathway as the impulses for voluntary gaze and the fast phase of vestibular nystagmus."[21]

Thus, if optokinetic targets move from the patient's left to right, the left occipital lobe will be activated and cause the eyes to deviate right. The right frontal lobe will then initiate the fast phase left to bring the eyes back to midline. Impulses travel from both occipital lobes to the frontal lobe via a pathway deep in the parietal lobe. There is anatomical evidence for such a pathway.[22] The predictions that follow and receive support are that:

1. For unilateral occipital lesions OKN will be normal. In cases of bilateral occipital lesions, OKN will be normal so long as some vision remains.

2. For both deep parietal lobe and diffuse frontal lobe lesions, OKN will be impaired to the side opposite the lesion. Lesions anywhere along the frontomesencephalic pathway from the frontal lobe to the brainstem may produce a deficit of the fast phase to the opposite side.

SUPPORT FROM ANIMAL RESEARCH

Detailed, scholarly discussion of the vestibular and oculomotor pathways in animal models are presented in Bender,[23] and Bach-Y-Rita et al.[24] We will not attempt a review of the literature in this section but will describe briefly a few investigations illustrating the effects of central lesions on OKN.

The role of both the cortex and thalamus on the integrity of OKN has been demonstrated by Neverov et al.[25] These investigators used the technique of spreading depression through microinjection of drugs into the parietal cortex or superior colliculus to blockade the functions of these structures during OKN or after-nystagmus. The subjects were eight rabbits placed securely in the center of an OKN drum (80 cm high by 140 cm in diameter) for testing. OKN was elicited during clockwise rotation of the drum at six revolutions per minute for 90 minutes. Frequency of OKN was markedly decreased by spreading depression in either the right hemisphere or right superior colliculus. By contrast, reduction in the activity of the left hemisphere or thalamus affected after-nystagmus.

Cohen[26] has shown the importance of the paramedian zone of the pontine reticular formation (PPRF) for normal OKN. Electrolytic lesions to the right PPRF resulted in changes in right-beating OKN. The quick phase was of relatively small amplitude, high frequency and low maximum velocity. There was a strong tonic deviation of the eyes to the left.

TABLE 1. DISTRIBUTION OF SUPRATENTORIAL LESIONS

Type	*No.*
Frontal mass lesion	3
Frontal-parietal mass lesion	2
Parietal infarction	5
Middle cerebral artery occlusion	5
Parietal-occipital infarction	2
Occipital pole infarction	1
Occipital mass lesion	1
Temporal mass lesion	4
Pontine infarction	1
Total	24

PRESENT INVESTIGATIONS

Rationale. While evidence may exist to support correlations between theoretical prediction and observation of eye movements in patients with well-documented lesions, the strength of OKN as a test for clinical diagnosis is not clear. Specifically, given a unilateral deficit of OKN, one may question the extent to which the result distinguishes two clinical groups with different sites of lesion. The data published are usually qualitative in nature, and the judgement of abnormality depends on a subjective evaluation by the examiner. To some extent his decision will reflect his knowledge of the results of clinical tests administered concurrently, and his own theoretical bias.

An attempt to collect quantitative data for various clinical groups was made by Morissette et al.[9] Their particular interest was the usefulness of OKN measurements for distinguishing peripheral from central vestibular lesions. Horizontal and vertical OKN in normal subjects and in patients with chronic unilateral labyrinthectomy and confirmed brainstem lesions were compared. The techniques of electronystagmography were used for documentation and analysis of response. Statistically significant differences between the normal and labyrinthectomy groups on the one hand and the brainstem group of the other suggested the value of the test for clinical otoneurological diagnosis.

The present study is a continuation of this work. The OKN of subjects in six groups are compared: normal subjects screened for vestibular disease, and patients with unilateral labyrinthectomy, Menière's disease, neurologically confirmed focal brainstem lesions, diffuse brainstem disease and radiologically confirmed supratentorial lesions. The focus of the work is an attempt to establish quantitative criteria for evaluating OKN in the diagnosis of peripheral vestibular and central nervous system lesions.

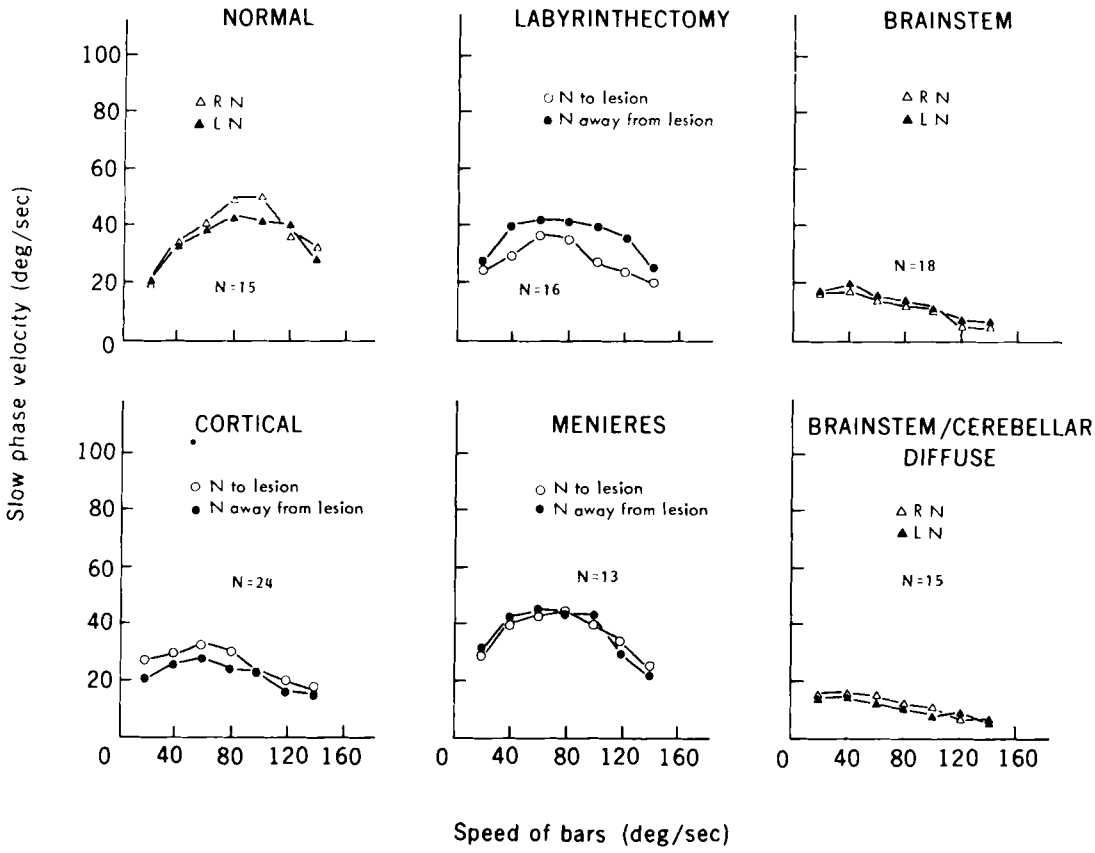

Fig. 1. Horizontal OKN.

METHODS

Subjects. One hundred and one paid volunteers served as subjects. All had normal vision, in some cases obtained with corrective lenses. They comprised six experimental groups:

1. Fifteen normal subjects, aged 18 to 39 years screened for otologic disease by routine audiometric and vestibular testing.

2. Sixteen patients with unilateral labyrinthectomy (11 right ear, 5 left), aged 31 to 72 years. The time lapse between surgical procedure and OKN test ranged between 1 and 52 months.

3. Thirteen patients with unilateral Menière's disease (6 right ear, 7 left), aged 33 to 72 years. In all cases the clinical diagnosis was based on unilateral vestibular reduction, fluctuating sensorineural hearing loss and severe episodic vertigo.[27]

4. Eighteen patients with neurologically confirmed brainstem lesions, 11 with infarction, 5 with multiple sclerosis, 1 with intrinsic neoplasm, and 1 with Arnold Chiari malformation, aged 27 to 85 years.

5. Fifteen patients with brainstem-cerebellar syndrome (eg, diffuse cerebellar degeneration, parkinsonism, encephalopathy of thiamine deficiency, neurofibromatosis) aged 27 to 90 years.

6. Twenty-four patients with focal unilateral supratentorial lesions with localization evident on radiologic examination, aged 25 to 76 years.

The distribution of lesions is given in Table 1.

Vestibular function was evaluated in each subject using a routine, standardized test battery. The battery included caloric testing, ie, irrigation of the two ears using hot (44 C) and cold (30 C) water, search for gaze nystagmus with lateral deviations of the eyes of 30° and vertical gaze directions of 10° from the primary eye position, examination of ocular tracking of a moving pendulum, and posture tests.[28] Eye movements were monitored and recorded using ENG.

Apparatus. The apparatus used for the experiment has been described previously.[9] During the OKN test, the subject was seated in a darkened room facing a translucent white screen at a distance of 80 cm. A circular field of parallel black bars covering 60° of visual angle was back-projected onto the screen. The bars were 5 cm wide and the distance between bars was 8.1 cm. The luminance of the ground was 1.75 foot-candles and the luminance gradient between the ground and bars was in the ratio of about 10:1.

The field of bars was produced by placing an opaque spiral drawn on a transparent disc between the condensor of a slide projector and a 35 mm wide angle lens. The disc was placed in the optical path of the projector in such a way that the rotary movement of the spiral would result in movement of the bars in a horizontal or vertical direction.

The speed of rotation of the disc was controlled by a feedback system in which the output from a potentiometer controlled by the experimenter and a tachometer were fed to a comparator. The speed of the motor driving the disc was increased or decreased depending on the voltage response of this comparator. A milliammeter connected to the tachometer was calibrated to read the speed of movement of the bars in degrees of visual angle per second ranging from 20 to 400. To avoid a stroboscopic effect, the projector was modified to work on direct current.

Eye movements were recorded using electronystagmography (AC coupling, time constant of five seconds), eyes separately and together in the horizontal axis and one eye in the vertical axis.

Procedure. Subjects were instructed to gaze at the surface of the screen. They were told to look at each bar as it passed the center point and to try not to follow any one bar as it moved from the center to the periphery of the visual field. In cases of response inhibition, subjects were instructed repeatedly to maintain a high level of attention.

The bars were projected successively at speeds ranging from 20

TABLE 2. MAXIMUM RESPONSE FOR HORIZONTAL OKN

Group		No.	Mean*	SD	Lowest Value	Highest Value
Normal	RN	15	59	25	22	122
	LN	15	55	20	28	101
Labyrinthectomy	N→L	16	46	17	25	77
	N←L	16	53	21	31	102
Menière's disease	N→L	13	49	12	31	70
	N←L	13	50	10	32	67
Brainstem	RN	18	20	11	3	38
	LN	18	22	9	7	43
Brnstm-cereb diffuse	RN	15	22	10	10	39
	LN	15	21	13	4	49
Cortical	N→L	24	38	14	7	67
	N←L	24	34	18	3	70

*Slow phase velocity in °/sec.

SD - Standard deviation; Brnstm-cereb - Brainstem-cerebellar; RN - Right-beating nystagmus (bars move left); LN - Left-beating nystagmus (bars move right); N→L - Nystagmus beating toward side of lesion; N←L - Nystagmus beating away from side of lesion.

to 140°/sec, in steps of 20°. Movement to the right and left of bars projected vertically were alternated for each speed. The procedure was repeated for the vertical axis, with a display of horizontal bars moving upwards and downwards.

At each speed (by direction) the display was presented for 20 to 30 seconds, the time required to observe at least one strong burst of nystagmus. If for any stimulus (speed by direction) no nystagmus was seen within 30 seconds, that presentation was discontinued and a zero recorded.

RESULTS

The response for each combination of direction of movement of the bars (right, left, up, and down) and bar speed (20°, 40°, 60°, 80°, 100°, 120°, 140°) was evaluated by measuring the slow phase velocity of OKN. The average value of the slope for the three fastest beats in the most easily identified group of beats persisting for at least five seconds was tabulated as the response.

HORIZONTAL OPTOKINETIC NYSTAGMUS

Figure 1 shows the average response plotted against bar speed for patients in the six groups. We have taken the liberty of labelling the supratentorial group as cortical, since in only one case was the lesion nonhemispheric. For normal subjects and those with brainstem lesions or diffuse brainstem-cerebellar disease the results are given separately for right-beating (RN) (bars move left) and left-beating (LN) (bars move right) OKN. For the other groups, labyrinthectomy, Menière's disease and supratentorial lesion, the laterality of the lesion was taken into account and the results are plotted separately for nystagmus beating toward (N → L) and away from (N ← L) the affected side, irrespective of the direction of movement of the bars.

Two distinct trends are apparent in these data. For normal subjects and those with chronic unilateral labyrinthectomy or Menière's disease, eye speed is a curvilinear function of bar speed, reaching a maximum for values of about 80°/sec. On the other hand, the brainstem and brainstem-cerebellar groups show a steady and gradual decline in eye speed for increases in stimulus speed. The data for patients with cortical lesions are midway between these two trends.

In order to compare the groups statistically, in a way which might prove useful for clinical diagnosis, we examined 1) the maximum value of slow phase velocity achieved by each subject, regardless of bar speed; 2) the bar speed giving the maximum response; and 3) the slow phase velocities obtained for relatively high and low bar speeds of 80° and 20°/sec, respectively.

Maximum Response. Table 2 shows the mean maximum response observed for subjects in each of the six groups. The standard deviation as well as the lowest and highest values of maximum response observed for the subjects in each group are given. Statistical comparison of the maximum response ob-

TABLE 3. RESULTS OF STATISITCAL COMPARISON OF MAXIMUM VALUES OF RESPONSE

	t	df	α
Within-group comparisons			
Labyrinthectomy			
N→L vs N←L	2.93	15	.050
Between-group comparisons			
Normal vs brainstem			
RN vs RN	6.03	31	.001
LN vs LN	6.29	31	.001
Normal vs cortical			
RN vs N→L	3.45	37	.010
N←L	3.77	37	.001
LN vs N→L	3.09	37	.010
N←L	3.45	37	.010
Labyrintectomy vs brainstem			
N→L vs RN	5.31	32	.001
LN	5.25	32	.001
N←L vs RN	5.99	32	.001
LN	5.93	32	.001
Labyrinthectomy vs cortical			
N→L vs N→L	NS		
N←L	2.17	38	.050
N←L vs N→L	2.86	38	.010
N←L	3.26	38	.010
Brainstem vs cortical			
RN vs N→L	4.32	40	.001
N←L	2.82	40	.010
LN vs N→L	4.10	40	.001
N←L	2.57	40	.050

NS - Not significant; N→L - Nystagmus beating toward side of lesion; N←L - Nystagmus beating away from side of lesion. Other abbreviations same as Table 2.

TABLE 4. DISTRIBUTION OF OBSERVED MAXIMUM SPEEDS

Maximum Slow Phase Velocity (°/sec)	*Normal* RN	LN	*Labyrinthectomy* N→L	N←L	*Menière's Disease* N→L	N←L	*Brainstem* RN	LN	*Brnstm-Cereb Diffuse* RN	LN	*Cortical* N→L	N←L
1- 10							4	2	1	3	1	1
11- 20							7	6	7	6	2	4
21- 30	2	1	3				3	7	3	3	4	9
31- 40	2	3	5	5	3	2	4	2	4	1	6	2
41- 50	0	3	1	3	5	3		1		2	7	3
51- 60	3	3	5	2	3	7					3	2
61- 70	4	2		4	2	1					1	3
71- 80	3	2	2									
81- 90				1								
91-100												
101-125	1	1		1								
Total No.	15	15	16	16	13	13	18	18	15	15	24	24

N→L - Nystagmus beating toward side of lesion; N←L - Nystagmus beating away from side of lesion. Other abbreviations same as Table 2.

served for left and right-beating nystagmus or for nystagmus beating to and away from the side of lesion within each group shows a significant difference only in the case of subjects with chronic unilateral labyrinthectomy. For this group the eye speed is higher when the nystagmus beats away from the side of the lesion.

Pairwise comparisons between the various groups show that the maximum response of patients with chronic unilateral labyrinthectomy or unilateral Menière's disease are not significantly different from those of normal subjects. On the other hand, the maximum response for patients with brainstem lesions or diffuse brainstem-cerebellar disease was significantly less than those for normals. The result for patients with cortical lesions fell midway between and was significantly different both from those of normal subjects and patients with brainstem findings.

In making the pairwise comparisons, the groups were compared on the basis of right-beating and left-beating nystagmus, taken separately. If lesion laterality was a factor for both groups then all four possible matches were made: nystagmus beating toward and away from the side of lesion in one group was compared with nystagmus beating toward and away from the side of lesion in the other group. If lesion laterality was known for only one of the two groups under comparison, then right and left beating nystagmus in the one group were each compared with nystagmus beating toward and away from the side lesion in the second group. The details of the *t*-tests are given for significant outcomes in Table 3. It should be noted that patients with Menière's disease and diffuse brainstem-cerebellar syndrome were included in the experiment to provide clinical controls for patients with chronic labyrinthectomy and focal brainstem lesions, respectively, and were compared only with these groups in this and subsequent analyses.

Table 4 shows the distribution of observed maximum speeds for all subjects. While significant differences were noted (see above) between the average values for the various groups, it is evident from this analysis that the ranges of values overlap considerably. Any choice of cut-off for decision making along the maximum slow phase velocity axis will be associated with some probability of error in diagnosis. Thus, for example, if a response of 30°/sec were to be chosen, 13% of normal subjects would be classified as abnormal (maximum less than 31°/sec) and 42% of cortical (N←L) and 22% of brainstem pa-

TABLE 5. BAR SPEED GIVING THE MAXIMUM RESPONSE FOR HORIZONTAL OKN

Group		*No.*	*Mean**	*SD*	*Lowest Value*	*Highest Value*
Normal	RN	15	81.3	29.7	20	120
	LN	15	89.3	28.1	40	140
Labyrinthectomy	N→L	16	65.0	33.1	20	140
	N←L	16	76.3	31.2	40	120
Menière's disease	N→L	13	70.7	24.0	40	120
	N←L	13	64.6	24.7	20	100
Brainstem	RN	18	40.0	25.7	20	100
	LN	18	43.3	25.0	20	100
Brnstm-cereb diffuse	RN	15	45.3	24.5	20	100
	LN	15	34.7	17.7	20	80
Cortical	N→L	24	50.8	22.8	20	100
	N←L	24	50.8	29.5	20	140

*Slow phase velocity in °/sec.

N→L - Nystagmus beating toward side of lesion; N←L - Nystagmus beating away from side of lesion. Other abbreviations same as Table 2.

TABLE 6. RESULTS OF STATISTICAL COMPARISON OF BAR SPEEDS GIVING THE MAXIMUM RESPONSE

	t	*df*	*α*
Within-group comparisons			
Labyrinthectomy			
N→L vs N←L	2.76	15	.050
Between-group comparisons			
Normal vs brainstem			
RN vs RN	4.29	31	.001
LN vs LN	4.97	31	.001
Normal vs cortical			
RN vs N→L	3.61	37	.010
N←L	3.13	37	.010
LN vs N→L	4.68	37	.001
N←L	4.04	37	.001
Labyrinthectomy vs brainstem			
N→L vs RN	2.48	32	.050
LN	2.17	32	.050
N←L vs RN	3.72	32	.001
LN	3.42	32	.010
Labyrinthectomy vs cortical			
N→L vs N←L	1.61	38	NS
N←L	1.42	38	NS
N←L vs N→L	2.98	38	.010
N←L	2.61	38	.050

NS - Not significant; N→L - Nystagmus beating toward side of lesion; N←L - Nystagmus beating away from side of lesion. Other abbreviations same as Table 2.

tients (RN or LN) would be called normal (maximum greater than 30).

Position of Maximum Response. The average value of bar speed for which the maximum response occurred is presented in Table 5. A summary of significant differences within and between groups is given in Table 6. The normal subjects and patients with labyrinthectomy are not different from each other in this analysis and the bar speed giving the maximum is between 65° and 90°/sec on the average for the two groups. For the brainstem group the maximum response occurs at a much slower bar speed of about 40°/sec. Patients with cortical lesions show a maximum response at a relatively higher speed of 50°. This is significantly different from the outcome for normal subjects but not from that observed for patients with brainstem disease.

OKN at Relatively High and Low Bar Speeds. In the last section, we demonstrated that normal subjects show a maximum slow phase velocity for a bar speed close to 80°/sec. A statistical comparison of the response was made both within and between subjects specifically for this bar speed. The data for a bar speed of 80° are given in Table 7 and the significant differences between groups are shown in Table 8. The trends observed are similar to those for maximum response given in Table 3.

To contrast the response for the various groups at high bar speeds, we compared the groups for the lowest bar speed. The significant comparisons are presented in Table 9. These data indicate that for a bar speed of 20°/sec the laterality of the lesion is important for patients with chronic unilateral labyrinthectomy and cortical lesions. For the former group the slow phase velocity is higher when the nystagmus beats faster away from the lesion and for the latter group, when the nystagmus beats in the direction of the lesion. An unexpected finding is the relatively greater response for these patients, when compared with that of normal subjects, regardless of the direction of nystagmus. By comparison, patients with brainstem lesions showed responses well within the normal range.

The distribution of results for the bar speed of 20°/sec are given for each of the groups in Table 10. Examination of right-beating nystagmus in normal subjects indicates that 11 of 15 give speeds between 16° and 25°/sec. Of the 13 patients with Menière's disease, 11 give speeds greater than 25° both for nystagmus beating to and away from the side of lesion. For 16 patients with labyrinthectomy 10 give slow phase velocities greater than the range when the nystagmus is beating away from the side of lesion.

Direction Preponderance of Maximum Response. In investigation of the peripheral vestibular system directional preponderance (DP) of eye movements in response to caloric stimuli is often used as a method for within-subject comparison of the two ears. Applying this logic to OKN[29] we calculated the difference in maximum slow phase velocity between right and left-beating nystagmus or between the maximum response for nystagmus beating toward

TABLE 7. RESPONSE FOR BAR SPEED OF 80°/SEC

Group		*No.*	*Mean**	*SD*	*Lowest Value*	*Highest Value*
Normal	RN	15	49	21	11	72
	LN	15	43	19	9	77
Labyrinthectomy	N→L	16	36	21	3	77
	N←L	16	42	22	11	83
Menière's disease	N→L	13	44	16	19	70
	N←L	13	44	14	12	63
Brainstem	RN	18	12	9	0	30
	LN	18	13	9	2	43
Brnstm-cereb diffuse	RN	15	13	11	1	39
	LN	15	13	13	1	49
Cortical	N→L	24	30	16	3	58
	N←L	24	25	18	2	70

*Slow phase velocity in °/sec.

N→L - Nystagmus beating toward side of lesion; N←L - Nystagmus beating away from side of lesion. Other abbreviations same as Table 2.

TABLE 8. SIGNIFICANT DIFFERENCES IN RESPONSE FOR BAR SPEED OF 80°/SEC

	t	*df*	α
Within-group comparisons	No significant differences		
Between-group comparisons			
Normal vs brainstem			
RN vs RN	6.97	31	.001
LN vs LN	6.09	31	.001
Normal vs cortical			
RN vs N→L	3.32	37	.010
N←L	3.78	37	.001
LN vs N→L	2.45	37	.050
N←L	2.98	37	.050
Labyrinthectomy vs brainstem			
N→L vs RN	4.34	32	.001
LN	4.11	32	.001
N←L vs RN	5.35	32	.001
LN	5.11	32	.001
Labyrinthectomy vs cortical			
N→L vs N←L	1.02	38	NS
N←L	1.62	38	NS
N←L vs N→L	2.02	38	.050
N←L	2.56	38	.050
Brainstem vs cortical			
RN vs N→L	4.12	40	.001
N←L	2.88	40	.010
LN vs N→L	3.84	40	.001
N←L	2.64	40	.050

NS - Not significant; N→L - Nystagmus beating toward side of lesion; N←L - Nystagmus beating away from side of lesion. Other abbreviations same as Table 2.

TABLE 9. SIGNIFICANT DIFFERENCES IN RESPONSE AT BAR SPEED OF 20°/SEC

	t	*df*	α
Within-group comparisons			
Labyrinthectomy			
N→L vs N←L	2.59	15	.050
Cortical			
N→L vs N←L	3.28	23	.010
Between-group comparisons			
Normal vs labyrinthectomy			
RN vs N→L	3.17	29	.010
N←L	3.83	20	.001
LN vs N→L	3.24	29	.010
N←L	3.89	29	.001
Normal vs Menière's			
RN vs N→L	5.82	26	.001
N←L	5.70	26	.001
LN vs N→L	6.29	26	.001
N←L	5.92	26	.001
Normal vs cortical			
RN vs N→L	2.76	37	.010
LN vs N→L	2.67	37	.050
Labyrinthectomy vs Menière's			
N→L vs N←L	2.96	27	.010
Labyrinthectomy vs brainstem			
N→L vs RN	3.22	32	.010
LN	3.71	32	.001
N←L vs RN	3.88	32	.001
LN	4.36	32	.001
Labyrinthectomy vs cortical			
N←L vs N←L	2.77	38	.010
Brainstem vs cortical			
RN vs N→L	3.51	40	.010
LN vs N→L	3.81	40	.001

N→L - Nystagmus beating toward side of lesion; N←L - Nystagmus beating away from side of lesion. Other abbreviations same as Table 2.

and away from the side of lesion, whichever was appropriate to the group. The mean differences are plotted for the six groups in Table 11, and it is evident that the values obtained are fairly similar. In the case of chronic unilateral labyrinthectomy, 12 of 16 patients show a higher maximum for nystagmus beating away from the side of lesion. For patients with Menière's disease, 8 of 13 show a DP favoring the side opposite the lesion. In contrast, 16 of 24 patients with cortical lesions show a higher maximum response for nystagmus beating toward the side of lesion.

CORTICAL LESIONS

Since much of the literature on OKN concerns the effect of the location of a cortical lesion, we attempted to subdivide our group of 24 patients with supratentorial lesions in terms of both locus and type of lesion. As indicated in Table 1, our sample consisted of 14 cases of infarction and 10 cases of mass lesion. Of the former group, 12 involved some area of the parietal cortex. In the latter group, two were anterior parietal. The location and type of lesion are highly related for our sample and thus, may not be evaluated separately.

Table 12 shows the range of maximum slow phase velocities observed for nystagmus beating toward (N→L) and away from (N←L) the side of lesion for the mass and infarction groups respectively. The median values are shown to allow a rough comparison. For the group of infarctions, the median value of maximum slow phase velocity for nystagmus beating away from the lesion has a value of 25. This is relatively low in comparison with the other values shown. However, a statistical comparison of the maximum values observed for individuals using the Mann-Whitney U test for unrelated samples shows no differences between mass and infarction groups either for nystagmus beating toward or away from the side of lesion.

A measure of directional preponderance (DP) was calculated for each subject using the difference between the maximum value of slow phase velocity observed for nystagmus beating toward and away from the side of lesion. The range of DP is given in Table 12 for the two groups. In the case of mass lesions, (nonparietal lobe) the value of DP is equally likely to be positive or negative and fairly symmetric about zero. On the other hand, for infarctions, (parietal lobe) in 12 of 14 cases the nystagmus beating away from the lesion is relatively diminished. Of the two exceptions, DP = 0 and −13, the latter value was obtained for the one patient who had sustained a stroke to the pons. Statistical evaluation of these data using the Wilcoxon test indicates that the average DP is significantly different from zero in the case of infarctions. The test takes into account the sign of relative magnitude of the difference observed for each subject. Under the null hypothesis of no directional bias the probability of the obtained outcome is 0.005. For mass lesions the probability was 0.5, ie, the results were highly likely given no expectation of a DP.

TABLE 10. DISTRIBUTION OF RESPONSE FOR BAR SPEED OF 20°/SEC

Slow Phase Velocity (°/sec)	Normal RN	Labyrinthectomy N→L	Labyrinthectomy N←L	Menière's Disease N→L	Menière's Disease N←L	Brainstem RN	Cortical N→L	Cortical N←L
1-5						1		1
6-10						4	1	0
11-15	3					3	2	3
16-20	4	2	3		1	3	1	8
21-25	7	9	3	2	1	3	8	7
26-30	1	4	6	5	2	3	3	2
31-35		0	2	4	5	1	5	2
35-40		1	1	2	3		3	0
41-45			1	0	1		1	1
Total No.	15	16	16	13	13	18	24	24

N→L - Nystagmus beating toward side of lesion; N←L - Nystagmus beating away from side of lesion. Other abbreviations same as Table 2.

VERTICAL OPTOKINETIC NYSTAGMUS

Figure 2 shows the average slow phase velocity as a function of bar speed for vertical OKN. Values for upbeating and downbeating nystagmus were analyzed separately.

Maximum Response. As for horizontal OKN, the maximum response observed across bar speeds was tabulated for each subject. Mean values of the maximum are shown for the six groups in Table 13. The significant statistical differences are given in Table 14. Within-group and between-group analyses were based on comparison of maximum slow phase values for up and down-beating nystagmus respectively. In making between-group comparisons lesion laterality was ignored.

These results show that for vertical OKN normal subjects give responses that are statistically greater than those for patients with brainstem or cortical lesions. The range of values for these groups, given by the lowest and highest scores in Table 13, indicate considerable overlap in response. For upward beating nystagmus, 9 of 17 subjects with localized brainstem disease fell below the range for normals and 8 within. For downward beating nystagmus only 6 subjects give values below the range and 11 give values comparable to those of normal subjects.

Vertical OKN at Low Speeds. The slow phase velocity observed for a bar speed of 20° was also examined. The average values for upward and downward beating nystagmus are presented in Figure 2. Significant comparisons are given in Table 15. Normal subjects give higher values for upbeating nystagmus than do patients with brainstem lesions. However, only 5 of 17 in the latter group are clearly below the normal range.

DISCUSSION AND CONCLUSIONS

The focus of interest of the present research has been the measurement of OKN for use in otoneurological diagnosis. In this regard the effect of a wide range of optokinetic target speeds on the slow phase velocity of OKN has been investigated both for horizontal and vertical target arrays. The groups tested were normal subjects and patients with well-defined peripheral vestibular lesions (chronic unilateral labyrinthectomy), focal brainstem lesions, and supratentorial tumor or infarction. Two additional groups, patients with Menière's disease and diffuse brainstem-cerebellar syndromes, were included on grounds of clinical relevancy. The etiology for these is often less clearly defined and we wondered how similar their performance would be to the patients with circumscribed lesions in the same areas, ie, labyrinthine and lower brainstem focus respectively.

We chose to isolate several features of the data for statistical analysis, with a view to defining quantitative criteria for routine clinical diagnosis. These were 1) the maximum slow phase velocity observed over the range of bar speeds used; 2) the bar speed at which the maximum response occurred; 3) the response at very low (20°/sec) and relatively high (80°/sec) bar speeds; and 4) the directional preponderance, or the difference in maximum response observed for nystagmus beating toward and away from the side of lesion. In an attempt to evaluate current theories of the neurological

TABLE 11. DIRECTIONAL PREPONDERANCE IN MAXIMUM SLOW PHASE VELOCITY

Group	No.	Mean Difference (°/sec)	SD	Lowest Value	Highest Value	No. of Subjects with No Difference
Normal	15	10	7	1	21	0
Labyrinthectomy	16	11	8	1	28	1
Menière's disease	13	9	7	1	20	0
Brainstem	18	9	8	1	26	4
Brnstm-cereb diffuse	15	6	4	2	13	1
Cortical	24	11	7	0	27	0

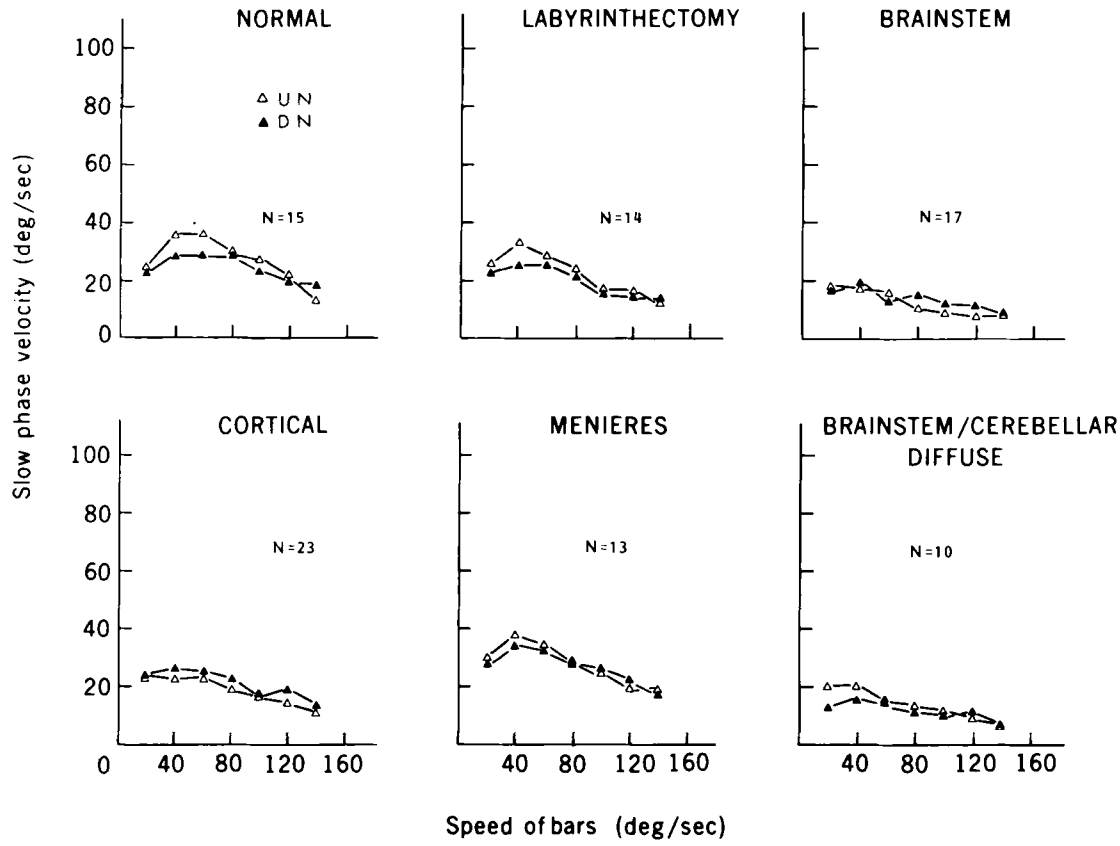

Fig. 2. Vertical OKN.

pathways subserving OKN we subsequently subdivided the cortical group for the purpose of studying the effect of the location (hemispheric lobe) and nature of the lesion (mass vs infarction) on OKN. Our findings indicate that for *horizontal* OKN:

1. The maximum slow phase velocity allows us to differentiate normal subjects and patients with unilateral labyrinthectomy on the one hand, from patients with focal brainstem lesions on the other. On the basis of this index, patients with Menière's disease were not unlike those with labyrinthectomy, nor could we distinguish brainstem-cerebellar syndromes from focal brainstem lesions. The average maximum slow phase velocity for patients with cortical lesions fell midway between the averages computed for normal subjects and patients with brainstem disease and was significantly greater than the value for the latter of these two groups.

2. The distributions of maximum response (ie, values observed in individuals) for groups which give significantly different results overlap considerably. We attempted to establish a cut-off value for use in the detection of abnormality and noted that the probability of false positives and negatives would be relatively high. Nevertheless, a maximum slow phase velocity of 30°/sec provides a crude yardstick. By this criterion, we find that 13% of normal subjects would be judged abnormal and 22% (about 1 in 5) of patients with brainstem disease would be judged normal.

3. Patients with chronic unilateral labyrinthectomy show a significantly lower maximum response for nystagmus beating toward the side of the lesion. However, the magnitude of the difference in each patient is 11° on the average and is similar to that observed for the difference between right and left-beating nystagmus in normal subjects.

4. The average bar speed at which the maximum response occurs is significantly greater for normal subjects (85°/sec) and patients with labyrinthectomy (70°/sec) than those with brainstem and cortical lesions. The position of maximum response for cortical lesions was 50°/sec on the average and this

TABLE 12. MAXIMUM RESPONSE FOR CORTICAL LESIONS

	No.	*N–L Range of Max. Resp.**	*Median*	*N–L Range of Max. Resp.*	*Median*	*Range of DP*
Mass lesion	10	24-58	42	20-70	38	−22 to 19
Infarction	14	7-67	38	3-55	25	−13 to 27

*°/sec.

N–L - Nystagmus beating toward side of lesion; N–L - Nystagmus beating away from side of lesion.

TABLE 13. MAXIMUM RESPONSE FOR VERTICAL OKN

Group		No.	Mean*	SD	Lowest Value	Highest Value
Normal	UN	15	41.3	12.6	24	78
	DN	15	36.9	9.6	15	50
Labyrinthectomy	UN	13	37.6	18.0	12	67
	DN	13	29.2	13.4	6	48
Menière's disease	UN	13	42.6	22.2	14	86
	DN	13	37.6	15.5	17	74
Brainstem	UN	17	20.9	12.4	6	40
	DN	17	21.4	8.5	6	31
Brnstm-cereb diffuse	UN	10	22.7	10.4	8	38
	DN	10	19.6	11.0	0	37
Cortical	UN	23	28.2	10.1	15	56
	DN	23	31.2	10.1	7	52

*Slow phase velocity in °/sec.

SD - Standard deviation; UN - Upbeating nystagmus; DN - Downbeating nystagmus.

was not significantly different from the value of 40° observed in the presence of brainstem lesions.

5. Analysis of the results obtained at a bar speed of 80°/sec yielded the same conclusions as those for analysis of the maximum responses (see Item 1 above).

6. At the slowest bar speed, 20°/sec, patients with lower brainstem lesions are not different from normal. However, patients with either peripheral vestibular disorders (labyrinthectomy or Menière's disease) or cortical lesions give eye speeds which are significantly greater than those of normal subjects and patients with focal brainstem lesions. This finding was unexpected and to our knowledge has not been previously reported. For both labyrinthectomy and cortical cases, lesion laterality is a significant factor. Specifically, for the former group eye speeds are higher for nystagmus beating away from the lesion (bars moving toward the side of lesion). For the latter group the eye speeds are higher for nystagmus beating toward the lesion. These data confirm the earlier findings of Davidoff et al.[19] In Menière's disease there were no significant within-group differences due to laterality.

7. While we find directional differences to be related to lesion laterality, the average value of 10° to 11°, as well as the highest and lowest value, are similar to normal. In patients with brainstem disease the average difference across patients as well as the highest observed value are smaller by a factor of two. These data suggest that on its own DP would not provide a good diagnostic index of abnormality. The range of values of DP for cortical lesions, both mass and infarctions (or parietal versus nonparietal lobe) are not different in absolute value from those of the other groups. However, in the case of infarctions we note that the direction of difference is significantly related to the laterality of the lesion (beating more strongly toward the lesion). In mass lesions it is unrelated.

For *vertical* OKN, lesion laterality was not taken into account and in all statistical comparisons the direction of nystagmus was held constant, either upbeating or downbeating.

The values observed for normal subjects are on the average 20° less than those for horizontal OKN. For brainstem subjects horizontal and vertical OKN are comparable. In terms of the maximum response observed for vertical OKN, normal subjects produce significantly higher values than do patients with focal brainstem lesions. Cortical lesions result in significantly lower values for upbeating but not downbeating nystagmus. A comparison of results between groups for a bar speed of 20° shows that the only group different from normal was the brainstem, but for upbeating not downbeating nystagmus.

TABLE 14. STATISTICAL COMPARISON OF MAXIMUM VALUES OF RESPONSE FOR VERTICAL OKN

	t	df	α
Within-group comparisons			
Labyrinthectomy			
UN vs DN	2.27	12	.050
Between-group comparisons			
Normal vs brainstem			
UN vs UN	4.61	30	.001
DN vs DN	4.87	30	.001
Normal vs cortical			
UN vs UN	3.56	36	.010
DN vs DN	1.76	36	NS
Brainstem vs cortical			
UN vs UN	2.03	38	NS
DN vs DN	3.24	38	.010

NS - Not significant. Other abbreviations same as Table 13.

TABLE 15. SIGNIFICANT DIFFERENCES IN VERTICAL OKN OBSERVED FOR A BAR SPEED OF 20°/SEC

	t	df	α
Within-group comparisons	No significant differences		
Between-group comparisons			
Normal vs brainstem			
UN vs UN	2.28	30	.05
DN vs DN	No significant differences		
Labyrinthectomy vs brainstem			
UN vs UN	2.13	29	.05
DN vs DN	No significant differences		
Brainstem vs cortical			
UN vs UN	2.16	38	.05
DN vs DN	2.16	38	.05

Abbreviations same as Table 13.

SUMMARY

The experimental results discussed above provide statistical confirmation for OKN findings previously reported in the literature. In summary, we find that compared with any other diagnostic category, the maximum slow phase velocity of OKN for the range of bar speeds studied is significantly reduced in patients with brainstem lesions. Patients with cortical lesions fall midway between the normal and brainstem groups and give significantly higher values on the average than the latter. Directional differences were investigated as an alert to the laterality of lesion and it was noted that in the case of chronic unilateral peripheral vestibular disease, nystagmus beat less strongly when the targets moved toward the lesion. The opposite was true for cortical infarctions located in the parietal region. An unexpected finding was the elevation in eye speed for very low target speeds in the case of patients with chronic unilateral labyrinthectomy and Menière's disease.

While the above conclusions are statistically significant, by itself the measurement of OKN is of limited use for purposes of clinical diagnosis. The distributions of observed maximum slow phase velocities for individuals in the various patient groups overlap considerably. The optimum criterion or cut-off value for decision-making leads to high error rates in predicting the presence of a lesion. While DPs were found to be related to the side of lesion for patients with either peripheral vestibular or cortical disease, the absolute size of the difference between the maximum slow phase velocity for nystagmus beating toward and away from the side of lesion was not different from the difference between left and right beating nystagmus in normal subjects.

ACKNOWLEDGMENTS — We are indebted to the vestibular technologists at Sunnybrook Medical Centre for their assistance in the testing of patients and analysis of ENG records, and wish to thank in particular Grace Wright, Antje Slessor, Lynn McIlmoyl and Carlos Dioknos. Special thanks are due to the staff of the Department of Neurosciences for making their patients available to us.

REFERENCES

1. Barany R. Zur Klinik und Theorie des eisenbahn-Nystagmus. Acta Otolaryngol (Stockh) 1922; 3:261.

2. Ohm J. Die klinische Bedeutung des optischen Dreyhnystagmus. Klin Monatsbl Augenheilkd 1922; 68:323.

3. Cords R. Optisch-motorisches Feld und optisch-motorische Bahn. Arch Ophthalmol 1926; 117:58.

4. Tos M, Adser J, Rosborg J. Horizontal optokinetic nystagmus in cerebral disease. Acta Neurol Scand 1972; 48:607-20.

5. Honrubia V, Scott BJ, Ward PH. Experimental studies of optokinetic nystagmus. I. Normal cats. Acta Otolaryngol (Stockh) 1967; 64:388-402.

6. Honrubia V, Downey WL, Mitchell DP, Ward PH. Experimental studies of optokinetic nystagmus. II. Normal humans. Acta Otolaryngol (Stockh) 1968; 65:441-8.

7. Honrubia V, Jenkins HA, Downey WL, Ward PH. Experimental studies in optokinetic nystagmus. III. Modifications produced by labyrinthectomy and hemidecortication in cats. Ann Otol Rhinol Laryngol 1971; 80:97-110.

8. Morissette Y, Abel SM, Barber HO. Optokinetic nystagmus: its value in the diagnosis of certain vestibular lesions. In: Guedry FE Jr, ed. The use of nystagmography in aviation medicine. AGARD Conf Proc No. 128, May 1973.

9. Morissette Y, Abel SM, Barber HO. Optokinetic nystagmus in otoneurological diagnosis. Can J Otolaryngol 1974; 3:348-62.

10. Smith JL. Optokinetic nystagmus: Its use in topical neuro-ophthalmologic diagnosis. Springfield: Thomas, 1963.

11. Baloh RW, Honrubia V, Sills A. Eye-tracking and optokinetic nystagmus: results of quantitative testing in patients with well-defined nervous system lesions. Ann Otol Rhinol Laryngol 1977; 86:108-14.

12. Ling W, Gay AJ. Optokinetic nystagmus: a proposed pathway and its clinical application. In: Smith JL, ed. Neuro-opthalmology. Vol. 4. St. Louis: Mosby, 1968.

13. Carmichael EA, Dix MR, Hallpike CS. Lesions of the cerebral hemispheres and their effects upon optokinetic and caloric nystagmus. Brain 1954; 77:345-71.

14. Cogan DG, Loeb DR. Optokinetic response and intracranial lesions. AMA Arch Neurol Psychiatry 1948; 61:183-7.

15. Kestenbaum A. Clinical methods of neuro-ophthalmologic examination. 2nd ed. New York: Grune and Stratton, 1961.

16. Smith JL. Homonymous hemianopia — A review of 100 cases. Am J Ophthalmol 1962; 54:616-23.

17. Smith JL, Cogan DG. Optokinetic nystagmus: a test for parietal lobe lesions. Am J Ophthalmol 1959; 48:187-93.

18. Smith JL, Cogan DG. Optokinetic nystagmus in cerebral disease — A study of 14 autopsied cases. Neurology 1960; 10:127-37.

19. Davidoff RA, Atkin A, Anderson PJ, Bender MB. Optokinetic nystagmus and cerebral disease. Arch Neurol 1966; 14:73-81.

20. Fox JC, Holmes G. Optic nystagmus and its value in the localization of cerebral lesions. Brain 1926; 49:333-71.

21. Gay AJ, Newman NM, Keltner JL, Stroud MH. Eye movement disorders. Saint Louis: Mosby, 1974.

22. Crosby E. Correlation anatomy of the nervous system. New York: Macmillan, 1962.

23. Bender MB, ed. The oculomotor system. New York: Harper and Row, 1964.

24. Bach-Y-Rita P, Collins CC, Hyde JE, eds. The control of eye movements. New York: Academic Press, 1971.

25. Neverov VP, Ueda M, Bures J. The effect of cortical and collicular spreading depression on the optokinetic and reversive postoptokinetic nystagmus in rabbits. Brain Res 1976; 115: 318-23.

26. Cohen B. Vestibulo-ocular relations. In: Bach-Y-Rita P, Collins CC, Hyde JE, eds. The control of eye movements. New York: Academic Press, 1971.

27. Alford BR. Report of subcommittee on equilibrium and its measurements. Menière's disease: criteria for diagnosis and evaluation of therapy for reporting. Trans Am Acad Ophthalmol Otolaryngol 1972; 76:1462-4.

28. Barber HO, Stockwell CW. Manual of electronystagmography. Saint Louis: Mosby, 1976.

29. Coats AC. Central and peripheral optokinetic asymmetry. Ann Otol Rhinol Laryngol 1968; 77:938-48.