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VESTIBULO-OCULAR REFLEX, OPTOKINETIC RESPONSE AND THEIR INTERACTIONS IN THE CEREBELLECTOMIZED CAT

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SUMMARY

1. The effects of total ablation of the cerebellum on eye movements were studied in alert adult cats.

2. The normal cat could easily hold a steady eye position after a saccadic movement in the dark. The cerebellectomized animal could not: after a saccade the eye position shifted towards a more central position. Vision reduced this 'post-saccadic drift'.

3. The sinusoidal vestibulo-ocular reflex (v.o.r.) was strongly affected by total cerebellectomy. In darkness the v.o.r. gain remained stable at high frequencies (0·5 and 1 Hz) but decreased markedly at lower frequencies to as low as 0·18 at 0·05 Hz. A phase advance (up to 65° at 0·05 Hz) paralleled this gain depression.

4. Velocity characteristics of optokinetic nystagmus (o.k.n.) and optokinetic after-nystagmus (o.k.a.n.) induced by constant-velocity full-field rotation of 60 deg/s amplitude and 60 s duration were studied. The features of o.k.n. (initial velocity, maximal velocity and time constant) were only mildly affected by cerebellectomy. On cessation of visual stimulation when the animal was plunged into darkness, the velocity of the eyes decreased progressively (o.k.a.n.). The time constant of o.k.a.n. was 12·5 s in the normal cat and 4·2 s in the cerebellectomized cat. Furthermore cerebellectomy abolished the secondary o.k.a.n.

5. Optokinetic response was also tested by a set of sinusoidal (0·05–1 Hz; 3–20°) full-field stimuli. The o.k.n. was not abolished but dramatically decreased, especially at higher frequencies. No response could be detected above 0·15 Hz.

6. Visual suppression of inappropriate vestibulo-ocular reflex was still possible but was mildly impaired after cerebellectomy. Visual suppression could only be detected with stimuli below 0·25 Hz.

7. Visual suppression of caloric nystagmus was studied in the normal cat. A clear dependence of the effectiveness of visual suppression on the velocity of the nystagmus was demonstrated.

8. In the cerebellectomized cat, the visual suppression of caloric nystagmus was lost when tested on nystagmus velocities above 20 deg/s but remained when tested on nystagmus velocities below 20 deg/s. The relationship between cerebellectomy and the loss of visual suppression of caloric nystagmus was found to be at least partially indirect: cerebellectomy increased the velocity of caloric nystagmus, and visual suppression was usually less effective at higher velocities.

INTRODUCTION

Qualitatively, the oculomotor syndrome of cerebellectomy is now well delineated. From experiments on the rabbit (Ito, Shiida, Yagi & Yamamoto, 1974), monkey (Westheimer & Blair, 1974; Takemori & Cohen, 1974*b*; Zee, Yamazaki, Butler & Gücer, 1981) and cat (Carpenter, 1972; Robinson, 1974; Keller & Precht, 1979) and from clinical observations (Baloh, Konrad & Honrubia, 1975; Zee, Yee, Cogan, Robinson & Engel, 1976; Avanzini, Girotti, Crenna & Negri, 1979; Estanol, Romero & Corvera, 1979) the following overview has emerged. Cerebellar ablation or dysfunction results in: (1) impaired ocular smooth pursuit movements (Westheimer & Blair, 1974; Estanol *et al.* 1979), (2) inability to generate high-velocity optokinetic nystagmus (o.k.n.) (Takemori & Cohen, 1974*b*), (3) failure to maintain eccentric gaze positions (Westheimer & Blair, 1974; Robinson, 1974), (4) some loss of the visual suppression of vestibular nystagmus (Ito *et al.* 1974; Takemori & Cohen, 1974*b*), (5) reduction of the sinusoidal vestibulo-ocular reflex (v.o.r.) gain at low frequencies (Carpenter, 1972; Keller & Precht, 1979), which is said to correspond to some deficit in the performance of the vestibulo-ocular integrator (Robinson, 1974), and (6) saccadic dysmetria (Ritchie, 1976).

Quantitatively, by contrast, major disagreements persist. It is not yet clear whether these discrepancies are due to interspecies differences or to different modes and/or ranges of testing. The present detailed study of the effects of total cerebellectomy on the ocular motility of the cat was therefore undertaken.

Special attention was paid to three questions. First, we wanted to understand the origin of the conflicting results of Takemori & Cohen (1974*b*) on the one hand and of Keller & Precht (1979) on the other. Takemori & Cohen (1974*b*) reported a virtually total loss of visual suppression of caloric nystagmus in the monkey after bilateral flocculectomy. In contrast Keller & Precht (1979) observed the persistence of some visual–vestibular interaction after total cerebellectomy in another species, the cat, and using another mode of vestibular stimulation.

The second major point concerned optokinetic processing. The pursuit capabilities of foveal species, especially man and the monkey, are twofold: the eye can voluntarily pursue a small moving target (smooth pursuit) or involuntarily follow a moving surrounding (o.k.n.). Cerebellectomy is reported to affect these properties differentially (Robinson, 1974; Estanol *et al.* 1979; Zee *et al.* 1981): there is defective smooth pursuit with relative preservation of the o.k.n. But it is worth pointing out that smooth pursuit was usually tested with a sinusoidal movement while o.k.n. was nearly always investigated by a step in velocity. In this paper we assess the effect of cerebellectomy on the o.k.n. by using a set of sinusoidal full-field stimuli.

The third problem dealt with in this paper concerns the effect of cerebellectomy on the integrators of the oculomotor system. Integration processing comes into play in the saccades (Keller, 1974), in the v.o.r. (Skavenski & Robinson, 1973) and in the optokinetic response (Collewijn, 1972). Cerebellectomy has been reported to decrease the performance of the saccadic integrator (Robinson, 1974) and the v.o.r. integrator (Carpenter, 1972). But the effect of cerebellectomy on the o.k.n. integrator has not been hitherto investigated.

METHODS

General procedure

Six alert cats (2·5–3·5 kg) were used in this study. All the techniques were chosen to cause a minimum of discomfort and no pain. The animals were implanted under general anaesthesia (dihydro-xylidino-thiazine (Rompun, Bayer) 3 mg/kg and pentobarbitone (Nembutal, Abbott) 20 mg/kg) and aseptic surgery with two chronic devices: a dental cement platform bolted to the skull for immobilizing the head and a pair of electrodes for horizontal electro-oculography (e.o.g.) recording. Experiments began at least 8 days after surgery. The animals were then trained to accept restraining conditions without stress. This was generally achieved in about 15 days. The cat's body was placed in a restraining box and its head immobilized via the skull implant. After a few weeks cats were so contented in the box that we had to maintain alertness by producing strange sounds. Eye movements were tested in the week before the operation and post-operatively on the third and the fourth days.

Recording eye movements

Eye movements were recorded by electronystagmography. Electrodes were implanted around the cat's bony orbit. The horizontal e.o.g. was measured across both eyes. Non-polarizable silver/silver chloride electrodes were used in order to reduce the d.c. drift. The leads from the electrodes (1 mm in diameter) to the plug socket were Teflon-insulated. Calibration was obtained by rotating the cat sinusoidally (at 0·5 Hz, 20°) when it was surrounded by a fixed lighted drum (Keller & Precht, 1979). The assumption was made that the peak-to-peak amplitude of the compensatory slow-phase eye movement (see section on Data Processing) was equal to the peak-to-peak amplitude of the head movement under these conditions of vestibular stimulation (Keller & Precht, 1979). Under the same conditions of eye adaptation, the fluctuations of this value from one day to another were less than 5%. As the e.o.g. varies with dark–light adaptation, some problems emerge when a calibration in the light is used for eye movements recorded in the dark. Therefore, in order to reduce dark adaptation and the resulting e.o.g. changes, the requisite periods of darkness were as short as possible and separated from each other by a 1 min illumination period. In this paradigm dark–light adpatation produced less than 5% fluctuation of the e.o.g. (Godaux, Gobert & Halleux, 1983*a*, Fig. 1). E.o.g. was calibrated at the beginning of the experiment and every 15 min thereafter. Experiments never lasted for more than 1 h. The movement of the rotating frame was monitored by a potentiometer. Rotating frame and e.o.g. signals were amplified by an AM 502 Tektronix amplifier with a bandpass d.c. to 100 Hz. They were subsequently recorded on a pen-writer (Hewlett Packard, Model 7402 A) and stored on magnetic tape (Phillips, Ana-Log 7).

Cerebellectomy

Cerebellectomy was performed aseptically under general anaesthesia (dihydro-xylidino-thiazine (Rompun, Bayer) 3 mg/kg and pentobarbitone (Nembutal, Abbott) 20 mg/kg) by gentle suction using an operating microscope. Dexamethasone (4 mg/day, I.M.) and antibiotics were instituted on the day of operation and continued for 3 days. Animals were killed under pentobarbitone (Nembutal, Abbott) anaesthesia on the fourth day, after testing, by intracardiac perfusion of 10% formalin. The completeness of the cerebellectomy was first confirmed with the aid of a dissecting microscope on the fixed brain. In addition brain sections were examined under a microscope to confirm total cerebellectomy and to rule out any other concomitant involuntary lesion. The brain stem was embedded in paraffin and serially sectioned every 5 μm. Every fiftieth section was stained with Haematoxylin and Luxol Fast Blue and examined. The atlas of Berman (1968) was used to help interpret the histological sections. Special attention was given to the vestibular nuclei. Cerebellectomy was found to be perfect in six out of twelve operated animals. Data from five animals with incomplete cerebellectomy and one animal with a vestibular lesion were discarded.

Stimulating device

The head of the cat was put in the centre of a turntable and placed so that the horizontal semi-circular canals were nearly horizontal (10° up with respect to the horizontal). The turntable could only move sinusoidally. It was surrounded by a drum (1 m diameter, 1 m high) the inner wall of which was covered with alternating white and black stripes (10° each). The drum could rotate either sinusoidally or at constant angular velocity. Furthermore the movements of the turntable and of the drum could also be mechanically coupled. A light within the drum could be turned on

or off during its rotation. To obtain a step-velocity optokinetic stimulus the drum was started up in complete darkness and the light was turned on for a given time once constant velocity was achieved.

Eye movement tests

(1) Spontaneous saccades were recorded in darkness and in the light.

(2) Sinusoidal v.o.r. was investigated in the dark and in the light. The only amplitude tested was 5° (one direction amplitude). Frequencies ranged from 0·05 to 1 Hz.

(3) The sinusoidal suppression of the v.o.r. (5° one direction amplitude; 0·05–1 Hz) was obtained when the turntable and the drum moved in the same direction, at the same speed.

(4) Sinusoidal optokinetic response was assessed by a set of sinusoidal movements of the drum. Each combination of five amplitudes (20°, 15°, 10°, 5° and 3°) and six frequencies (0·05, 0·10, 0·15, 0·25, 0·5 and 1 Hz) was used.

(5) O.k.n. was also measured during rotation of the drum at a constant velocity for 60 s. At the end of the rotation the light was turned off to record o.k.a.n.

(6) Caloric nystagmus was induced by a unilateral cold-water irrigation of 100 ml infused over a period of 30 s. Temperatures between 3 and 30 °C were used. The light was then turned off for 40 s during which time the nystagmus developed; afterwards the light was turned on for several periods of 15 s until the nystagmus vanished. The restraining frame was tilted so that the horizontal canals were placed at 80° with respect to the ground. Once again the animal was trained to accept the stimulus conditions.

Data processing

For sinusoidal (vestibular or optokinetic) stimuli, the slow cumulative eye position curves were constructed manually from the raw records (Meiry, 1966). Gain was defined as the ratio of peak-to-peak eye position to peak-to-peak rotating frame position. Phase shift was designated as zero when eye and head movements were exactly opposite for the v.o.r. and exactly similar for the o.k.n. Eight to ten cycles were used.

The o.k.n. and o.k.a.n. induced by constant-velocity full-field rotation were analysed by measuring the velocity of the slow phases, once each second. The dominant time constant of slow phase velocity curves (o.k.a.n.) were estimated by the ratio of total eye deviation during o.k.a.n. to peak velocity of o.k.a.n. (Cohen, Matsuo & Raphan, 1977).

RESULTS

Effect of cerebellectomy on horizontal saccades

Normal cats could hold their eyes steady after a saccade even in the dark (Fig. 1*A*). When a cerebellectomized cat made a saccade towards the periphery in the dark, its eyes drifted back towards a more central position (Fig. 1*B*). This drift has an exponential profile, so that a time constant T of the movement could be defined. T was measured for ten horizontal post-saccadic drifts in each cat. The mean value ($\pm$standard deviation) was $1{\cdot}44 \pm 0{\cdot}44$ s (the individual values ranged from 1·28 to 1·75 s). These features were modified when vision was allowed (Fig. 1*C*): horizontal post-saccadic drift developed for 0·5–1 s but was followed by a roughly steady eye position. Quick resetting phases of the v.o.r. and o.k.n. were also followed by such a slipping movement (Fig. 1*D*). In subsequent frequency domain analyses small amplitudes (5°) were used as often as possible in order to reduce the frequency of the quick phases. Furthermore, post-saccadic parts of the v.o.r. or o.k.n. curves were not taken into account in building the slow cumulative eye position (Fig. 1*D*).

Effect of cerebellectomy on the optokinetic response

We studied the optokinetic response to a step of velocity of 60 deg/s and of 60 s duration (Fig. 2). The o.k.n. was tested twice clockwise and twice counterclockwise

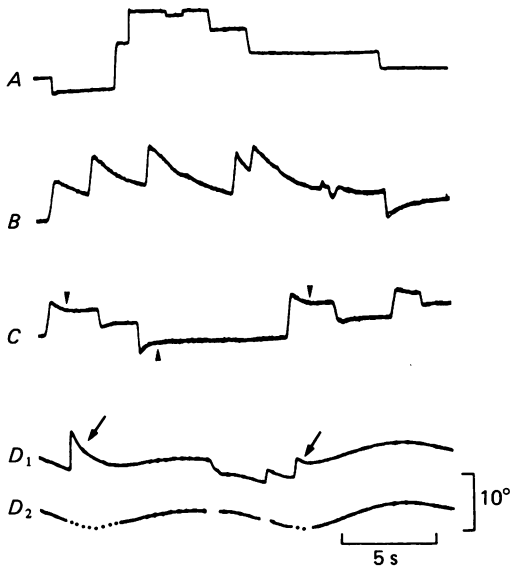

Fig. 1. *A–C*, spontaneous saccadic eye movements performed by a normal cat in the dark (*A*), by a cerebellectomized cat in the dark (*B*) and by a cerebellectomized cat in the light (*C*). Note the post-saccadic drift in *B*. In the light (*C*), this drift is rapidly over. The arrowheads point to the end of the post-saccadic drifts.

D_1–D_2, vestibulo-ocular reflex (v.o.r.) in a totally cerebellectomized cat (5°, 0·10 Hz). D_1 is the raw trace, D_2 is the cumulative slow eye position extracted by hand. Note the overlooking of the saccadic phases and of the post-saccadic drift periods (arrows) in the building of the D_2 curve.

in each of three cats. This procedure was applied both before and after cerebellectomy. In normal cats, the velocity of the slow phases of o.k.n. rose rapidly to $3{\cdot}8 \pm 1{\cdot}4$ deg/s. This initial rise in velocity was followed by a more gradual increase to the steady-state value. The measured maximal velocity was $26{\cdot}8 \pm 3{\cdot}4$ deg/s (Fig. 2*C*). The mean time constant of the gradual increase was $14{\cdot}9 \pm 3{\cdot}9$ s. When the light was turned off, the velocity of the slow phases (o.k.a.n.) decreased roughly exponentially with a time constant of $12{\cdot}5 \pm 6{\cdot}8$ s. After a velocity step of 60 deg/s and of 60 s duration, the o.k.a.n. always showed two phases: the first phase was in the same direction as during the o.k.n. (primary o.k.a.n.); the second phase was oppositely directed (secondary o.k.a.n.) (Fig. 2*B*, upper trace).

After cerebellectomy, the o.k.n. showed a rapid initial rise to $4{\cdot}3 \pm 1{\cdot}8$ deg/s. Afterwards the slow phase velocity increased with a time constant of $11{\cdot}3 \pm 6{\cdot}0$ s to a maximal steady value of $23{\cdot}7 \pm 5{\cdot}7$ s. The o.k.a.n. rapidly decreased with a time constant of $4{\cdot}2 \pm 1{\cdot}2$ s. None of our twelve post-cerebellectomy o.k.a.n. traces showed secondary o.k.a.n. (Fig. 2*B*, lower trace). Fig. 2*C* displays the calculated mean o.k.n. and o.k.a.n. curves. Table 1 shows the different parameters of o.k.n. and o.k.a.n. for three cats. We found no major modification of the o.k.n. by cerebellectomy. The initial rise of velocity, the time constant of o.k.n. and the maximal steady-state velocity were not consistently (see Table 1) or statistically ($P < 0{\cdot}05$) modified by cerebellectomy. In contrast, the o.k.a.n. was found to be drastically changed by cerebellectomy. Both the time constant of the o.k.a.n. and its duration were consistently (see Table 1) and statistically ($P < 0{\cdot}001$) reduced by cerebellectomy.

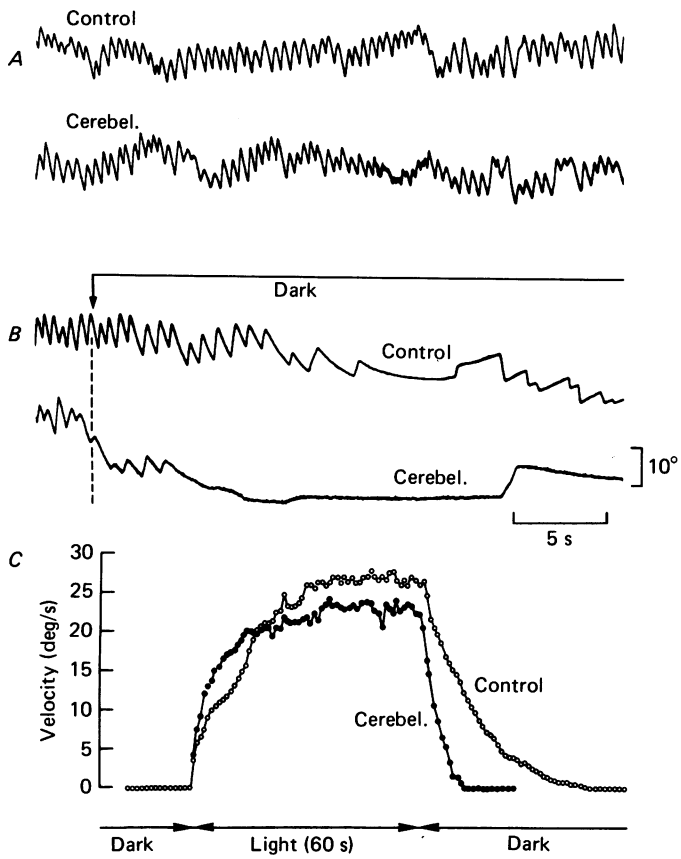

Fig. 2. Optokinetic response to a step of velocity of 60 deg/s and of 60 s duration. *A*, steady-state optokinetic nystagmus (o.k.n.) in one cat before (above) and after (below) cerebellectomy. *B*, optokinetic after-nystagmus (o.k.a.n.) in one cat before (above) and after (below) cerebellectomy. Note the presence of the secondary after-nystagmus in the normal cat and the lack of it in the cerebellectomized cat. *C*, Mean o.k.n. and o.k.a.n. curves obtained by averaging twelve raw curves measured on three cats. Negative values measured during secondary o.k.a.n. are not taken into account for averaging. Note the decreased time constant of o.k.a.n. after cerebellectomy.

Optokinetic function was also assessed by a set of sinusoidally moving stimuli. Fig. 3 illustrates the experiments on one cat. In the normal cat o.k.n. gain was about 1 at lower frequencies and decreased with frequency augmentation at each tested amplitude (Godaux *et al.* 1983*a*). In the cerebellectomized cat the o.k.n. gain diminished slightly at lower frequencies and dramatically at higher frequencies: above 0·25 Hz no o.k.n. response was observable (Fig. 3*D–F*). In Fig. 4 are plotted the average gain and phase of the optokinetic response as a function of frequency and amplitude for four experiments on four cats. Fig. 4*A* and *B* display the results before and after cerebellectomy respectively. Both in the normal and in the cerebellectomized cat, an increasing phase lag paralleled the lowering of the gain (Fig. 4).

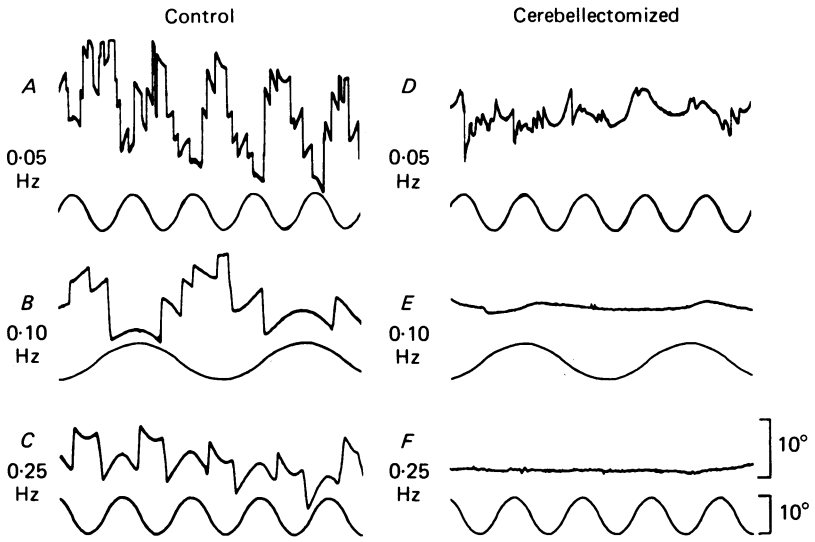

Fig. 3. Optokinetic response to sinusoidal full-field stimuli in one cat before (*A–C*) and after (*D–F*) cerebellectomy. In each block are displayed the eye movement (e.o.g. signal, upper trace) and the optokinetic drum movement (lower trace).

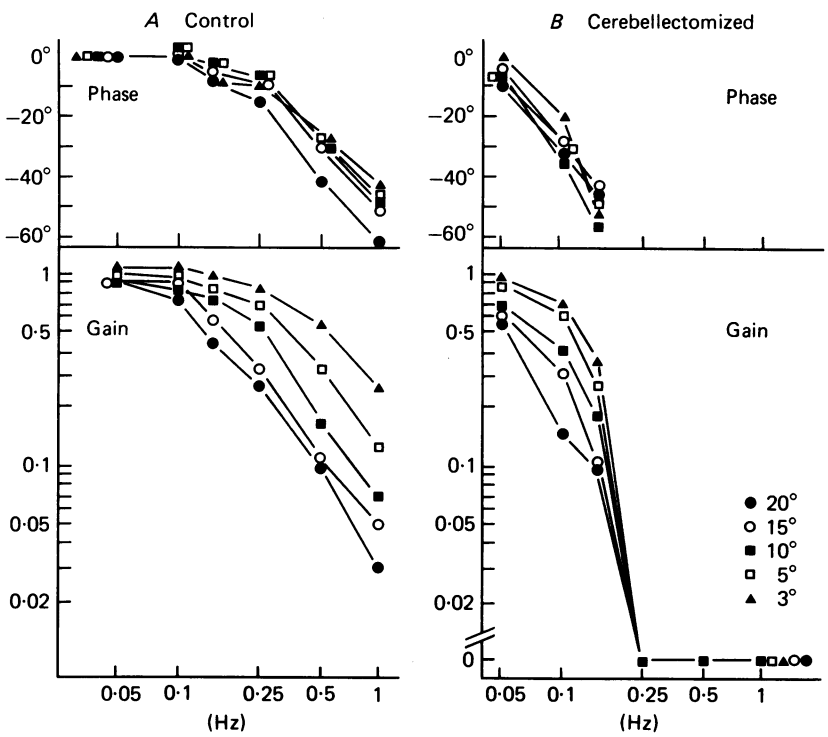

Fig. 4. Gain and phase of the optokinetic response as a function of frequency (Bode plot) before (*A*) and after (*B*) cerebellectomy. These values are plotted for different amplitudes as specified. Average values of four experiments on four cats. Note the interruption of the logarithmic scale on the ordinate. Negative phase values correspond to phase lag.

TABLE 1. Parameters of the optokinetic nystagmus and optokinetic after-nystagmus

(a) The optokinetic nystagmus (o.k.n.)

	Control			Cerebellectomized		
	Initial velocity (deg/s)	Time constant (s)	Steady-state velocity (deg/s)	Initial velocity (deg/s)	Time constant (s)	Steady-state velocity (deg/s)
Cat 9	3·6±0·9	13·0±3·8	27·7±3·9	5·2±1·5	6·8±2·3	29·6±3·7
Cat 10	5·0±1·0	17·6±3·4	27·6±1·8	5·2±0·9	18·2±1·9	20·5±2·5
Cat 12	2·8±0·4	14·1±3·7	25·1±5·1	2·5±1·3	8·9±4·2	21·0±4·7

(b) The optokinetic after-nystagmus (o.k.a.n.)

	Control			Cerebellectomized		
	Time constant (s)	Duration (s)	Presence of secondary o.k.a.n.	Time constant (s)	Duration (s)	Presence of secondary o.k.a.n.
Cat 9	11·3±3·0	28·5±7·3	+	4·1±1·6	10·0±3·7	−
Cat 10	17·5±9·3	41·3±21·6	+	4·8±0·5	10·8±1·7	−
Cat 12	8·7±3·0	22·6±8·2	+	3·7±1·7	10·7±3·6	−

TABLE 2. Gain of the vestibulo-ocular reflex (v.o.r.) in the cerebellectomized cat: vestibular–visual interactions

Frequency (Hz)	V.o.r. dark				V.o.r. light				V.o.r. suppression			
	Cat 2	Cat 6	Cat 9	Cat 10	Cat 2	Cat 6	Cat 9	Cat 10	Cat 2	Cat 6	Cat 9	Cat 10
0·05	0·20	0·15	0·14	0·23	0·66	0·80	1·00	1·00	0·12	0·14	0	0
0·10	0·40	0·28	0·23	0·32	0·48	0·86	1·00	0·80	0·26	0·21	0	0
0·15	0·40	0·50	0·29	0·32	0·38	0·86	1·00	0·60	0·38	0·29	0·01	0
0·25	0·43	0·90	0·36	0·31	0·54	0·94	0·70	0·58	0·64	0·63	0·21	0·38
0·5	0·90	1·00	0·70	0·48	0·98	1·20	1·00	0·56	0·90	1·10	0·68	0·52
1	1·20	1·00	0·92	0·72	1·20	1·28	1·00	0·68	1·02	1·30	0·96	0·66

Effect of cerebellectomy on the sinusoidal v.o.r.

Fig. 5*A* and *D* show two examples of v.o.r. in the dark after cerebellectomy. The gain is as low as 0·20 in *A* (cat 2, 0·05 Hz) and 0·23 in *D* (cat 9, 0·10 Hz). Fig. 6 shows the Bode plot of the 5° amplitude v.o.r. in the dark. The graphs correspond to the mean values obtained in four experiments in four cats before (Fig. 6*A*) and after (Fig. 6*B*) cerebellectomy. In the normal cat the gain was about 1 at 1 Hz and tended to diminish slightly at lower frequencies. A definite phase lead (around 35°) was also observed. In the cerebellectomized cat the gain remained unchanged at higher frequencies but diminished markedly at lower frequencies to as low as 0·18 at 0·05 Hz. An increased phase lead to 65° paralleled this low gain. These results are similar to those of Keller & Precht (1979). Table 2 shows the individual variability of the gain in the v.o.r. in the cerebellectomized cat.

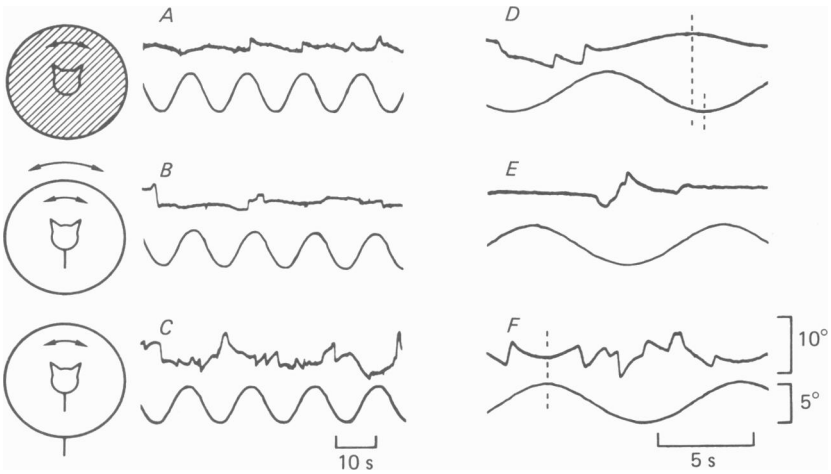

Fig. 5. Sinusoidal visual–vestibular interactions in two totally cerebellectomized cat. The Figure shows the v.o.r. in the dark (*A* and *D*), under suppression conditions (*B* and *E*) and in the light (*C* and *F*). *A–C* illustrate the v.o.r. in response to a 5° and 0·05 Hz stimulus in one cat. *D–F* show the v.o.r. in response to a 5° and 0·10 Hz stimulus in another cat. The upper trace of each block corresponds to the eye movement (e.o.g. signal). The lower trace indicates the movement of the rotating device (turntable in *A* and *D*, both turntable and optokinetic drum in *B* and *E*, optokinetic drum in *C* and *F*). *A–C*, recording from cat 2; *D–F*, recording from cat 9 (see Table 2).

Effect of cerebellectomy on the sinusoidal moment-to-moment visual–vestibular interaction

The sinusoidal v.o.r. gain observed in the dark (v.o.r. dark) could be modified moment-to-moment when vision was allowed in the normal cat. When the v.o.r. of the normal cat was tested in a stationary lighted environment, a considerable improvement in gaze stabilization was observed (v.o.r. light). However, when the striped drum moved in phase with the turntable, the surrounding remained stationary relative to the cat's head. The v.o.r. gain then was diminished (v.o.r. suppression) (Fig. 6*A*) (Godaux, Halleux & Gobert, 1983*b*).

Fig. 5 shows two examples of maintenance of visual–vestibular interaction in the cerebellectomized cat. Fig. 5*A–C* shows the improvement of the v.o.r. gain in the light

at 0·05 Hz. The v.o.r. gain is 0·20 in darkness and increases to 0·66 in the light. Suppression of v.o.r. is less marked in this case. Fig. 5*D–F* shows for another cerebellectomized cat at another frequency (0·10 Hz) the influence of vision on the v.o.r. The gain of v.o.r. in darkness (0·23) increases to 1 in the light and decreases to 0 in the suppression condition. Fig. 6 displays the v.o.r. gain and phase as a function of frequency both in the normal (Fig. 6*A*) and in the cerebellectomized (Fig. 6*B*) cat

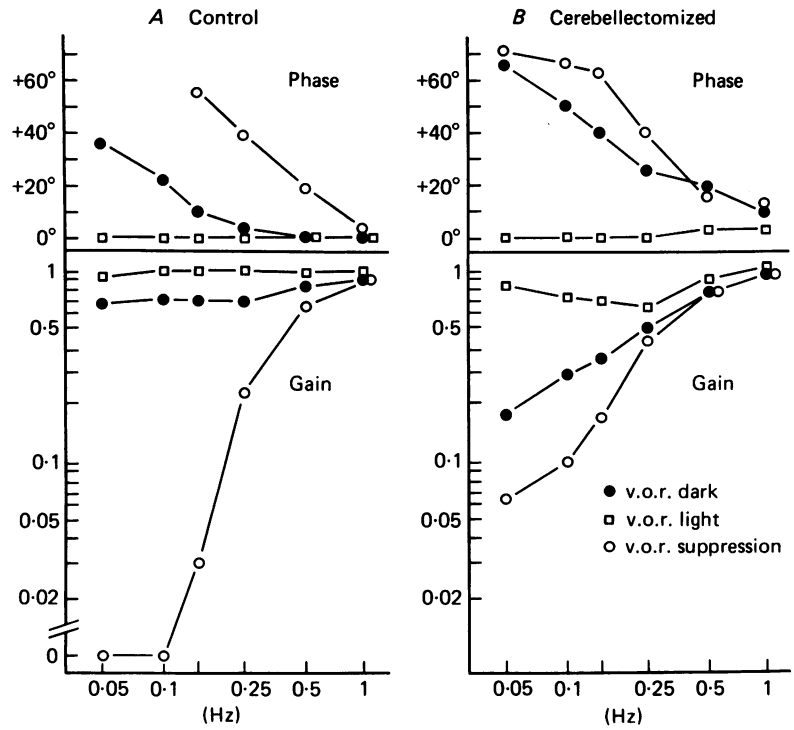

Fig. 6. Gain and phase of the vestibulo-ocular reflex (v.o.r.) as a function of frequency (Bode plot) before (*A*) and after (*B*) cerebellectomy. The plotted values correspond to three different conditions of testing: basic v.o.r. tested in the dark (filled circles), v.o.r. tested in the light (open squares) and v.o.r. suppressed by vision (open circles). The tested amplitude is 5°. Notice the interruption of the logarithmic scale on the ordinate. Average values of four experiments on four cats. Positive phase values correspond to phase lead.

for the dark, the light and the suppression conditions. Table 2 displays the corresponding individual gain values in the cerebellectomized animal. Comparison of Fig. 6*A* and *B* shows that the visual v.o.r. suppression persists but is less strong in the cerebellectomized cat. At 0·05 Hz the mean value of the v.o.r. gain in the dark fell from 0·65 to zero in the suppression condition in the normal cat and from 0·18 to 0·06 in the cerebellectomized cat. Modification of the v.o.r. in the light was also evident in the cerebellectomized cat: the v.o.r. gain increased from 0·18 to 0·88 at 0·05 Hz. Furthermore the phase lead was reduced concomitantly from 65° to 0°. This improvement in phase was complete in the cerebellectomized animals over the whole frequency range.

Effect of cerebellectomy on caloric nystagmus

Caloric nystagmus was induced by cold-water irrigation of the right ear in three cats. After irrigation, the light was turned off. The nystagmus developed gradually, reaching its maximal velocity in about 30–40 s. This value was maintained at a relatively constant level for a variable period. Afterwards, the slow phase velocity gradually diminished over a few minutes. After irrigation with water at 3 °C the velocity reached 19·2±9·7 deg/s in the normal cat. The maximal velocity of slow phases tended to decrease as caloric stimuli were made weaker, i.e. much closer to 38 °C. Visual suppression of caloric nystagmus was induced by allowing vision during

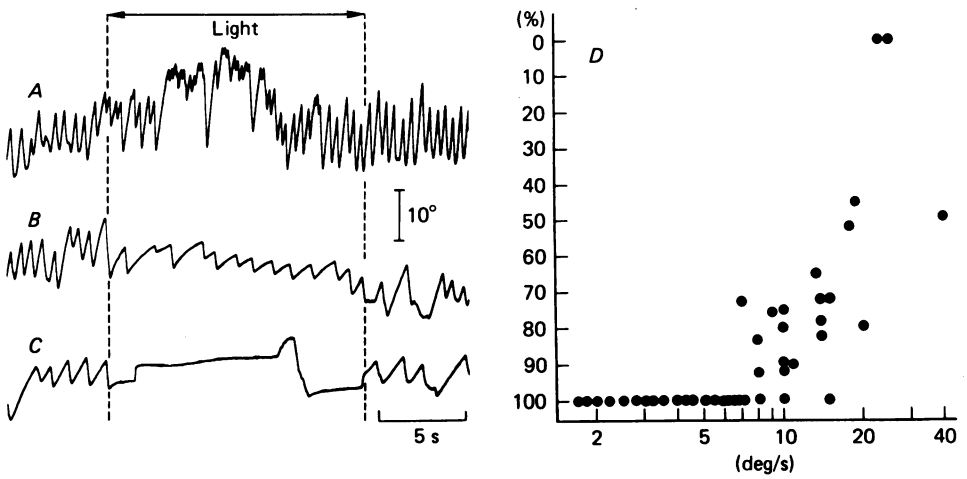

Fig. 7. Visual suppression of caloric nystagmus: dependence of the percentage of visual suppression on the intensity of nystagmus in the normal cat. In *A*, the caloric nystagmus induced by irrigation with water at 3 °C has a velocity of 24 deg/s; the corresponding percentage of visual suppression is zero. In *B*, the nystagmus velocity is 13 deg/s whereas the percentage of visual suppression is 72%. In *C*, the caloric nystagmus induced by irrigation with water at 23 °C has a velocity of 6 deg/s; the corresponding visual suppression is complete (100%). *D*, the percentage of visual suppression (ordinate) of caloric nystagmus as a function of slow phase nystagmus velocity (abscissa). Pooled data from four cats.

a 15 s period. Visual suppression was tested first at the maximal velocity (40 s after the end of irrigation) and every 45 s thereafter. This procedure was applied to irrigation at several water temperatures. The dependence of visual suppression on the intensity of the nystagmus could thus be assessed. Visual suppression was defined as the ratio (in per cent) of the mean slow phase velocity at the end of the fixation period to the slow phase velocity in the dark, just before visual fixation. Fig. 7*A–D* illustrates the dependence of visual suppression on the intensity of the nystagmus in one cat. Fig. 7*D* shows the pooled results from fifteen experiments on four cats. The visual suppression was virtually total when the velocity of the nystagmus was less than 7 deg/s. Above 7 deg/s the percentage of suppression tended to diminish as the velocity of nystagmus increased.

After cerebellectomy, the intensity of the nystagmus was greater: after irrigation

with water at 3 °C the maximal velocity was 31·2 ± 10·0 deg/s. Visual suppression was totally lost for nystagmus velocities greater than 20 deg/s (Fig. 8*E*) but persisted for velocities less than this (Fig. 8*E*). Fig. 8*A* and *B* illustrate the maximal caloric nystagmus and the corresponding visual suppression during irrigation with water at 3 °C in one cat before (Fig. 8*A*) and after (Fig. 8*B*) cerebellectomy. Before cerebellectomy the maximal velocity was 10 deg/s and the visual suppression was 90 %. After cerebellectomy the same cat showed a maximal velocity of 20 deg/s with a virtual loss of visual suppression (Fig. 8*B*). However, if visual suppression was tested during the vanishing phase of the caloric nystagmus or on a caloric nystagmus induced by water temperatures closer to body temperature, i.e. on lesser velocity nystagmus, visual suppression remained possible (Fig. 8*C*, *D*). Fig. 8*A* and *C* illustrate the fact that when a caloric nystagmus of similar velocity was induced in the normal (10 deg/s, Fig. 8*A*) and the cerebellectomized cat (11 deg/s, Fig. 8*C*), the corresponding visual suppressions were similar (90 % in Fig. 8*A* and 73 % in Fig. 8*C*).

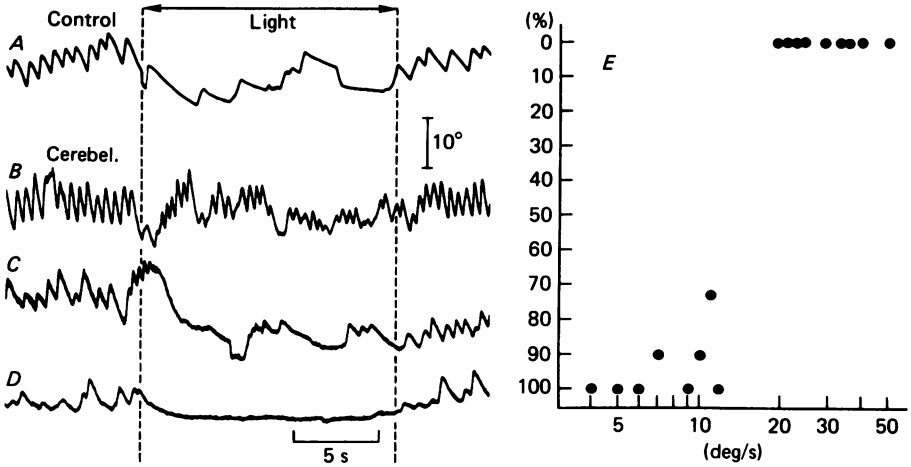

Fig. 8. Visual suppression of caloric nystagmus in the cerebellectomized cat. *A*, percentage of visual suppression (ordinate) as a function of the slow phase nystagmus velocity (abscissa): *A–D*, examples of visual suppression of caloric nystagmus in one cat before (*A*) and after (*B–D*) cerebellectomy. The velocity of the slow phase of the nystagmus is 10 deg/s in *A*, 20 deg/s in *B*, 11 deg/s in *C* and 6 deg/s in *D*. The corresponding percentage of visual suppression are 90 % (*A*), 0 % (*B*), 73 % (*C*) and 100 % (*D*).

DISCUSSION

The visual–vestibular interaction

Suppressive effects of visual fixation on vestibular (spontaneous in disease, post-rotatory and caloric) nystagmus are well known (Frenzel, 1955; Aschan, Bergstedt & Stahle, 1956). In 1974, Ito and co-workers on the one hand, and Takemori & Cohen on the other, proposed a neural basis for visual suppression: the flocculus would be the locus of visual–vestibular interaction. Ito *et al.* (1974) claimed that v.o.r. suppression was absent when tested with a sinusoidal stimulus (10°, 0·10 Hz) in the flocculectomized albino rabbit. A similar result was reported in the flocculectomized chinchilla (Daniels, Hassul & Kimm, 1978) and Dutch rabbit

(Honrubia, Koehn, Jenkins & Fenton, 1982). Takemori & Cohen (1974*b*) described a virtual loss of visual suppression of caloric nystagmus after flocculus lesions in the monkey.

This theory was, however, challenged by Keller & Precht (1979) who demonstrated in the cat that improvement of the v.o.r. in the presence of vision remained after total cerebellectomy. Furthermore the fact that the very large majority of vestibular nuclei neurones related to the horizontal semi-circular canals respond to pure optokinetic stimulation, has now been demonstrated in the goldfish (Dichgans, Schmidt & Graf, 1973; Allum, Graf, Dichgans & Schmidt, 1976), monkey (Waespe & Henn, 1977) and cat (Keller & Precht, 1979). The same result is obtained after cerebellectomy (Keller & Precht, 1979).

In this paper we have extended the results of Keller & Precht (1979) to the suppression condition: suppression of the sinusoidal v.o.r. at low frequencies was still possible in the cerebellectomized cat. Furthermore we found that visual suppression of caloric nystagmus is still present in the cerebellectomized animal when the velocity of the slow phases of the nystagmus is low (less than 20 deg/s). At higher velocities, visual suppression is dramatically lost in both normal and cerebellectomized cats. We have also demonstrated that the velocity of nystagmus is an important parameter for visual suppression in the normal cat. Furthermore, a similar unilateral cold-water irrigation evoked a higher-velocity nystagmus in the cerebellectomized cat. The relationship between the lack of visual suppression of nystagmus and cerebellectomy in the cat (Takemori, 1975) is thus at least partially indirect: cerebellectomy increases the velocity of caloric nystagmus and visual suppression is usually less effective at higher velocities.

The visual suppressive effect roughly parallels the optokinetic capabilities (Baarsma & Collewijn, 1974; Batini, Ito, Kado, Jastreboff & Miyashita, 1979; Godaux *et al.* 1983*a*) and the slow phase of optokinetic nystagmus can reach velocities in excess of 100 deg/s in the monkey (Cohen *et al.* 1977) but does not exceed 30 deg/s in the cat. One would expect a narrower velocity range for the visual suppressive effect in the cat. We have found this to be the case.

Our results stress the point that the conflict between the results of Takemori & Cohen (1974*b*) and Keller & Precht (1979) is not due to interspecies differences but rather to different ranges of testing. This view is strengthened by a recent finding by Ito, Yastreboff & Miyashita (1982) that visual improvement of v.o.r. is still possible in the flocculectomized albino rabbit at lower frequencies (0·05 Hz) than were tested in their earlier work (Ito *et al.* 1974).

In summary, our findings indicate that the basic visual–vestibular interaction does not take place in the cerebellum and that the cerebellum only improves the quality of that interaction.

The optokinetic system

It has been reported repeatedly that cerebellar lesions affect the ability to track small targets more than the ability to generate slow phases of o.k.n. (Zee *et al.* 1976; Estanol *et al.* 1979). From these observations it has been inferred that smooth pursuit and not the o.k.n. requires the help of the cerebellum (Estanol *et al.* 1979). However, as pointed out in the Introduction, the difference in question might be due to different

modes of testing. The usual stimulus for smooth pursuit is a sinusoidally moving small target, while a step of velocity is used to assess the optokinetic function.

In this paper, o.k.n. was tested with a set of sinusoidal full-field stimuli. We demonstrated that o.k.n. was not abolished but dramatically decreased, especially at higher frequencies. No optokinetic response could be detected above 0·15 Hz. It was not hitherto realized that cerebellectomy affects differently the optokinetic response to a step of velocity and the optokinetic response to sinusoidal full-field movements: the first is only slightly impaired while the latter dramatically decreases. This result is of particular interest because it was obtained in a species with poor capability for smooth pursuit. The foveate animal, even when submitted to a full-field optokinetic stimulus, tends to fixate a particular point so that a partial failure of o.k.n. might reflect a deficit only of the smooth-pursuit movement. In the cat a failure of the smooth-pursuit system following cerebellectomy could not affect the result, as its smooth-pursuit capability is very poor (Evinger & Fuchs, 1978).

In summary, our results indicate that basically the o.k.n. is not mediated by the cerebellum, though the cerebellum improves optokinetic function especially at higher sinusoidal frequencies. This is consistent with the micro-electrode studies of Waespe and Henn in the vestibular nuclei (Waespe & Henn, 1977) and flocculus (Waespe & Henn, 1981) of the monkey.

The integrators of the ocular motricity

The current interpretation of post-saccadic drift was proposed by Robinson in 1974. The holding of position after a saccadic change of position corresponds to an integration in the mathematical sense of the word. There would be a saccadic integrator located in the pons (Cohen & Komatsugaki, 1972; Luschei & Fuchs, 1972). But it is a leaky integrator with a time constant of only 1·3 s. The cerebellum somehow improves the performance of this integrator by raising its time constant above 20 s (Robinson, 1974).

The neuronal network of the v.o.r. must also involve an integrator because the firing frequency of the primary vestibular afferents is proportional to head angular velocity while the output of the system (i.e. the firing frequency of the ocular motoneurones) is proportional to both the angle of the eye and its angular velocity (Skavenski & Robinson, 1973). Functionally this implies the existence of an integrator in the vestibulo-ocular pathway. Cerebellectomy caused a phase advance and a marked gain decrease at lower frequencies. This is the result the control theory would predict if cerebellectomy dramatically affects the performance of the v.o.r. integrator.

Convergence of labyrinthine and visual inputs on the secondary vestibular neurones makes these an essential link in the optokinetic pathway. As a corollary, visual information must reach the ocular motoneurones through the vestibulo-ocular network: that is through the direct pathway and through the 'integrator pathway'. In other words, an integrator is shared by the v.o.r. and the optokinetic pathways. As the time constant of this vestibulo-ocular integrator is shortened by cerebellectomy, one would expect the time constant of the optokinetic integrator to be affected similarly. The time constant of the optokinetic integrator is better assessed by the time constant of the o.k.a.n. Indeed, on cessation of visual stimulation, when the animal is plunged into darkness (o.k.a.n.), no visual feed-back can come into action,

so that the integrator operator can be more easily assessed, without the complication of a closed-loop condition. One would thus expect the time constant of the o.k.a.n. to be shortened by cerebellectomy, and this was indeed the case in our study.

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