ON NYSTAGMUS AND OTOLITHS

A VESTIBULAR STUDY OF RESPONSES AS
PROVOKED BY A CEPHALO-CAUDAL HORIZONTAL
AXIAL ROTATION

J. B. JANEKE

1968

JANEKE / ON NYSTAGMUS AND OTOLITHS

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PROMOTOR:

PROF. DR. L.B.W. JONGKEES

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ACADEMISCH PROEFSCHRIFT

TER VERKRIJGING VAN DE GRAAD VAN DOCTOR IN DE GENEESKUNDE AAN DE UNIVERSITEIT VAN AMSTERDAM, OP GEZAG VAN DE RECTOR MAGNIFICUS MR. J. VAN DER HOEVEN, HOOGLERAAR IN DE FACULTEIT DER RECHTSGELEERDHEID, IN HET OPENBAAR TE VERDEDIGEN IN DE AULA VAN DE UNIVERSITEIT (TIJDELIJK IN DE LUTHERSE KERK, INGANG SINGEL 411, HOEK SPUI) OP DONDERDAG 4 JULI 1968 DES NAMIDDAGS TE 4.00 UUR

door

JOHAN BENJAMIN JANEKE

geboren te Pietermaritzburg, Natal
Republiek van Zuid Afrika

1968

DRUKKERIJ CLOECK EN MOEDIGH N.V.
AMSTERDAM

Dit proefschrift werd bewerkt in het klinisch-fysiologisch laboratorium van de afdeling Keel-, Neus- en Oorheelkunde, Wilhelmina Gasthuis, Amsterdam.

26/6/68.

Beste Egbert

Vir jou raad & vriendskap in & buite die ziekenhuis is ek innig dankbaar

Aan my vrou, ouers en skoonouers

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VOORWOORD

Dit is vir my 'n voorreg om die vele persone te bedank wat vir my in die geleentheid gestel het die studie te kan voltooi.

Aan my ouers bly ek altyd dankbaar vir alles wat hulle vir my gedoen het in die loop der jare.

Aan die Hoogleerare en dosente van die Pretoriase Universiteit bly ek dankverskuldig vir my mediese onderrig.

Hooggeleerde Jongkees, seergeagte promotor. Dit is vir my 'n groot eer gewees, om onder u leiding die ondersoek te kan verrig. Sonder u inspirasie en diepgaande kennis van die vestibulêre orgaan het die studie nooit totstand gekom.

Seergeleerde Oosterveld; u entoesiasme en aangename medewerking was 'n deurslaggewende faktor tydens die opbou van hierdie werk.

Seergeleerde de Boer; u fisiese kennis en kritiese nasien van my manuskrip was van besondere groot hulp.

Seergeagte van der Laarse; u toewijding en konstruktiewe bydrae het vele tegniese probleme oorbrug.

Hooggeleerde Groen en Seergeleerde James; u belangstelling en bydrae word "hogelijk" waardeer.

Seergeleerde Hammelburg en Seergeleerde Heron; onder u bekwame leiding het ek my eerste kennis opgedoen in die vak.

Seergeagte Hertz en Seergeagte Bakker; wees oortuig van my dankbaarheid vir die meganiese en fotografiese hulp.

Aan my mede assistente is ek dankbaar vir die aangename samewerking.

Aan die verplegende personeel en die staf van die laboratorium en gehoorsaal: die prettige werksklimaat en goeie sfeer sal ek altyd onthou.

Seergeleerde Pfeifers en Seergeagte Ek; u matematiese bydrae het lig gebring in die duisternis van formules.

Dr. Benson and Bodin; I would like to express my gratitude towards the inspiring visit to your laboratory at Farnborough.

Vir die uiters goeie behandeling van die proefdiere en hulp bedank ek mnre. Varenhorst en Zwaaf.

My geliefde eggenote; die totstandkoming van die werk is mede aan jou te danke.

INTRODUCTION

As early as 1932 Veits remarked that we can only study labyrinthine physiology under unphysiological conditions. Jongkees (1944), added to this remark that rotational stimuli (about a vertical axis) specifically designed to provoke labyrinth responses even perfected to the refined modifications such as subliminal stimuli (Veits 1931) are still unphysiologic. The same author is of the opinion that even provocation of nystagmus is already calling for an unphysiologic response (Jongkees 1964).

Most of the current stimuli applied to study labyrinth responses are directed either to the canals or otoliths. This allows separate studies of both the sub-organs, e.g. the post-rotatory or parallel-swing responses. The former were described by Bárány in 1907 and were later modified by Veits 1931, (the so-called subliminal stimuli directed to the canal system). Van Egmond, et al 1948, perfected these principles to cupulometry (Hulk and Jongkees, 1950; Van Egmond, et al 1949; Jongkees 1954 and Groen 1954). Variations of the latter technique lead to the torsion swing. This is less complicated and easier to apply (Mach 1875; Van Egmond et al 1949; Hennebert 1961, 1965; De Boer et al 1963; Pignataro and Dittrich 1963; Sokolovski 1963; Jongkees and Philipszoon 1964 and Oosterveld, 1963, 1965, 1967). The rotational stimulus is about a vertical axis and allows us to assess the reaction of the pair of semicircular canals in a plane perpendicular to the axis of rotation. A pure cupular response is provoked and the otolith organs are not stimulated at all. Otolith responses, on the other hand, can be studied by means of the parallel swing; it supplies the proper stimulus which consists of an oscillating linear acceleration and deceleration (Mach 1875; Groen and Jongkees 1947; Philipszoon 1959, 1962; Jongkees and Philipszoon 1960, 1962; Walsh 1960; Bos, et al 1962 and Jongkees 1963, 1964, 1966 and 1967) to the otoliths.

Remarkably, this idea was mentioned by Mach in 1875 in his monograph "Grundlinien der Lehre von den Bewegungsempfindungen". As far as we know the parallel swing provokes a pure otolith response.

The above principles are so well studied and investigated that a point near saturation is reached. Little more information, it seems, can be obtained to solve the remaining peripheral-labyrinth problems by these techniques alone. For further studies on labyrinthine physiology it is necessary to apply more complex stimuli in order to investigate some of the unexplained labyrinth responses, e.g. the coriolis stimulus*. (Wojatschek 1909; Schubert 1931, 1936; Meda 1952; Krause 1960; Bornschein and Schubert 1961; Arslan 1961; Guedry and Montique 1961; Dowd 1965 and Janeke and Jongkees 1968;

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*Coriolis G.G. Traité de la mécanique des corps solides et de calcul de l'effet des machines. Paris 1829.

Collins 1968 and Solodovnik, et al 1968.) Schubert attributed this force to the name of the French physicist Coriolis, who in 1845 studied from a purely physicists point of view, the complemental acceleration which acts on a subject submitted simultaneously to a rotatory and a translational motion relative to the rotation axis. (This reaction occurs when a subject, exposed to a constant angular velocity displaces his head along any axis not parallel to the axis of rotation.) This stimulus brings about a complex of objective manifestations since canals and otoliths are stimulated simultaneously.

The barbecue rotation is another example which produces simultaneous stimulation of both sub-organs. This name is commonly used for a rotation about a horizontal axis. It implies that a test animal (or subject) is rotated about its longitudinal axis in a horizontal plane. It was relatively late introduced by Benson 1962. (Lorente de Nó 1931 was the first to rotate animals about a horizontal axis. The longitudinal body axis was 30 cm from the rotation axis. This is not simular to a barbecue rotation for the rotation distance can evoke a centrifugal force which is not the case during a barbecue rotation). Later the barbecue rotation was also studied by Guedry 1964; Correia and Guedry 1964, 1966; Benson 1962, 1967; Benson and Bodin 1965, 1966; Janeke and Jongkees 1967/68; Janeke and Oosterveld 1968; Janeke and Kaminszczik 1968. In principle this kind of stimulation differs from the abovementioned group. First it differs from a pure rotational stimulation because the rotation is about a horizontal axis and not about a vertical one. This introduces alteration in the position of the labyrinth with respect to gravity. Second it differs from the parallel-swing stimuli because the direction of gravity alternates through 360°, clockwise or counter-clockwise. This submits the various canal- and otolith planes (utricular and saccular) to a continuous change in the direction of gravity. The modulation effects of both sub-organs on each other can now be investigated. One must bear in mind that the barbecue rotation is not an acceleration per se, but rather a constant rhythmic reorientation to the gravity direction (Guedry 1964).

LITERATURE REVIEW

In 1820 Purkinje observed nystagmus in man following a rotation stimulus; to our knowledge for the first time. In 1842 Flourens attributed nystagmus to the labyrinths and in 1861 Ménière considered vertigo and labyrinth pathology as related to one another. Reviewing the literature there are two trends of thought on the proper stimuli for the suborgans of the labyrinth, viz:

a) The canal system responds to linear and angular accelerations. This view was held by Magnus and De Kleijn (1921). They differentiated between a "static" and "dynamic" linear acceleration (Progressivbewegungen), the former percepted by the otoliths and the latter by the canal system. Lorente de Nó (1931) was also of the opinion that the membranous canals as such could be displaced by lineair acceleration.

Ter Braak (1936); Gernandt (1950) and Timm (1953) regarded the cupula as having a greater specific gravity than the surrounding endolymph. (In contrary to Trincker (1962) who regards the cupula as having the same specific gravity as the endolymph). The latter fact would render the cupula sensitive to linear accelerations.

Vogel (1951 and 1960) blocked the lateral semicircular canals in patients with positional nystagmus and vertigo, because this author was of the opinion that the canal system is gravity sensitive.

Benson and Whiteside (1961); Benson (1962) and Benson and Bodin (1965 and 1966) regarded the difference in the specific gravity (Dähnhardt 1869 and Kaieda 1930) between endo- and perilymph (1.0204 and 1.0200 respectively) as a factor which could render the canal system gravity-sensitive. Benson in 1967 reconsidered his opinion and stated that the canal system is not stimulated by the action of gravity.

Money and Scott (1962), Nito et al (1964) and Money et al (1965) are of the opinion that the canals are rendered gravity sensitive by intoxication with alcohol.

The above authors ascribe it to a cupular mechanism. The exact mechanism of alcohol nystagmus is not known (Rothfeld 1913; De Kleijn and Versteegh 1930; Bos et al 1963; Jongkees and Philipszoon 1963; Aschan et al 1964).

b) The canal and otolith system respond to different forms of accelerations the socalled Mach-Breuer theory (1875 and 1874). They were of the opinion that the canals and the otoliths are stimulated by angular and linear accelerations (gravity). Ewald in 1892 stated that the canals are responsible for nystagmus and that the direction of the eye- or headmovements correspond to the plane of the stimulated canals.

The question whether or not the canals can respond to a linear acceleration and gravity touches the basic principles of labyrinthology.

Convincing work in this field appeared by Jongkees (1944, 1964, 1966, 1967);

Groen and Jongkees (1946) and Philipszoon (1959, 1962). They described the physiological stimulus and the corresponding responses for each of the sub-organs separately; that the otolith-organs (the utriculus and sacculus) respond to linear accelerations and gravity and not to angular accelerations and that the six semicircular canals respond to angular accelerations and not to linear accelerations or gravity.

The finding that nystagmus can also be provoked by linear accelerations (Jongkees and Philipszoon 1962) makes it acceptable that the semicircular canals are not the only generators of nystagmus.

The latter fact suggests that otoliths can also influence the appearance of nystagmus.

Reviewing the literature we see that a number of authors are of diverging opinions about the question whether or not nystagmus could originate from the otoliths.

Bárány (1921) stated that positional nystagmus originates from the otolith organs, but did not exclude the possibility of a central origin.

Borries (1925) was the first to describe an otolithic-ocular reflex. He, incorrectly as it appeared later, thought that nystagmus was the result of caloric stimulation of the otoliths, and even suggested that the semicircular canals were not important for a caloric reaction (Versteegh still found nystagmus after saccular destruction and severing of the utricular nerve).

Maxwell (1923) found that if pressure was applied on the otolith so as to move the otolith slightly inwards, it produced eye deviations but no nystagmus.

Nylén (1925) suggested the name "otolithic disease" for postural vertigo and nystagmus. (So did Bergstedt and Herberts, 1962).

Versteegh (1927) did not observe nystagmus after destruction of the sacculus and the utricular nerve.

Sjöberg (1931) studied the effects of linear acceleration in lifts and recorded eye movements by means of a photokymograph. He was not able to record any definite nystagmus but he stated that he saw suggestions of it in several of his subjects and concluded therefore: "It is extremely probable that small reflex eye movements, invisible to the naked eye, occur in the case of rectilinearly accelerated vertical eye movements".

Ulrich (1934) produced eye deviations but not nystagmus in the unanaesthetized pike by direct stimulation of the utricular otolith with a human hair. The pressure of the hair was approximately 1.7 mg. as determined theoretically by Steinhausen (1934). Displacement or extirpation of the saccular otoliths produced neither eye deviations nor nystagmus.

Löwenstein (1949) performed some experiments on an isolated otic capsule of the thornback ray. By using micro-electrode relay methods he postulated several observations inter alia, that: "the otolith organs show a clear reaction to linear translations in the three planes of space". He did not mention the presence of nystagmus.

Jongkees (1949) found that pressure on the sacculus membrane by means of a steel ball which was introduced into the inner ear of rabbits and exposed to a magnetic field produced head movements but no nystagmus. In 3 out of 29 rabbits a lesion of the inferior part of the labyrinth caused positional nystagmus. Szentagothai (1952) performed direct mechanical stimulation of the otoliths in dogs and cats. He observed eye deviations but no nystagmus.

Dix and Hallpike (1952) reported on a patient with positional nystagmus of the benign paroxysmal type. At the post mortem examination they found remarkable pathological changes in the utricular macula and they concluded that positional nystagmus is a disease caused by utricular disorders. This conclusion seems not very well founded since in the brain stem of the patient metastases of a malignant tumour were found.

Graybiel et al (1952) found that in normal subjects the increase of the gravitational (resultant) force in a centrifuge did not produce nystagmus.

Morimoto (1955) carried out several neuro-physiological experiments on rabbits and cats. He subjected cats to an angular rotation while recording signals from the canal and otolith nerve fibres. He found signals which would indicate an activity of both sub-organs and concluded that interaction of canal and otolith systems is necessary for the appearance of nystagmus.

Citron and Hallpike (1956) reported cases of positional nystagmus of the socalled "benign paroxysmal type", whose origin they ascribe to lesions of the otolith apparatus.

Sullivan, et al (1957) sectioned the utricular nerve in cats. They did not notice the appearance of spontaneous nystagmus following the operation.

In contrast to Versteegh (1927); Jongkees (1950); Sullivan et al (1957);, Fernandez et al (1959) were able to produce spontaneous nystagmus in cats by sectioning of the utricular nerve, although they could not provoke nystagmus by stimulation of it.

Hallpike and Pfaltz (1960) studied more than 100 patients with positional nystagmus of the "benign paroxysmal type". They are convinced that the lesion is within the labyrinth, and probably in the otolith apparatus.

Owada et al (1960) provoked nystagmus by mechanical pressure upon the utriculus in rabbits. They also found a directional preponderance in the caloric test after section of the utricular nerve.

Bergstedt (1961) could not elicit nystagmus in his experiments with linear accelerations. He used lifts, cars, and a large centrifuge for human subjects. On the other hand he clearly showed an influence of linear accelerations on pre-existent positional nystagmus which increased under the influence of larger "g's".

Bergstedt and Herberts (1962) removed the otoliths by means of suction in a patient suffering from Ménière's disease and an accompanying positional nystagmus. The authors concluded that the disturbances lay in the otolith mechanism. They hope in the future to extract the otoliths without damaging the cochlea and canal functions.

Sakata (1962) studied labyrinth reflexes in 12 normals and 54 patients. He concluded that observation of the counter-rolling of the eyes was important, not only for the knowledge of the function of the otoliths, but also to understand the mechanism of the "rotatory nystagmus" related to the otolith organs.

Benson (1962, 1967), Correia and Guedry (1964, 1966), Guedry (1964) and Benson and Bodin (1965 and 1966) provoked nystagmus by using a constant barbecue rotation. Benson at first attributed this recorded nystagmus to a cupular action (Benson's "slosh theory")*[1], later as an interplay between otolithic and central processes. This had been suggested at an earlier date by Miehlke (1955) who found histological proof for his view that a disturbance in the cooperation of otoliths and cupulae would lead to positional nystagmus. McCabe (1964) demonstrated a clear nystagmus when subjecting cats, chinchillas and humans to rhythmic linear accelerations. He considered the nystagmus response as of otolith origin.

More work in this field appeared by Jongkees and Philipszoon (1961, 1962), Philipszoon (1962), Bos et al (1962) and Jongkees (1964). Nystagmus was provoked by linear accelerations on a parallel swing. When rabbits were placed on their sides or humans looked to either extremes, nystagmus appeared. The parallel swing produces an appropriate stimulus for otolith stimulation (Jongkees 1944, Groen and Jongkees 1946 and Jongkees 1964, 1966).*[2]

Yokoyama (1965) subjected normal rabbits and humans to linear accelerations. He used macroscopic observation and electronystagmography. The rabbits showed counter-rolling of the eyes on stimulation in a direction of the body axis and a vertical eye deviation if stimulated in the bi-temporal axis. The vestibular-ocular reflex was present in linear accelerations of 9 cm/sec.^{2} Rabbits with total destruction of their labyrinths, however, did not show any eye movements when stimulated. No comment was issued whether the canals or otoliths were responsible for the nystagmus.

Niven et al (1966) provoked a horizontal nystagmus in subjects subjected to linear accelerations directed along the subjects left-to-right ear axis. No comment is given on the etiology of the nystagmus.

To our present knowledge, only the otoliths are stimulated by a linear acceleration. It appears that when stimulated, the otolith organs can lead to the formation of nystagmus beats.

The basic principles of nystagmus provoked by a linear acceleration, are explained as follows by Jongkees and Philipszoon (1962).

Nystagmus consists of two components viz a slow and fast phase. Each of these has its own threshold (Jongkees and Philipszoon 1964). When the eye position is deviated by either a cupula or an otolith stimulation, the threshold for a quick phase is reached and a nystagmus beat is formed. (Alexander's law 1929). The quick phase is then in an opposite direction to that of the eye position. This view is also held by Guedry (1964) and Groen (1967). They term the quick phase component as a "saccadic repositioning" of the eye from an extreme deviation.

In spite of the many observations and ingenious experimental work regarding the function of the vestibular organ, we are anything but satisfied with our present knowledge. Modern labyrinth studies need the cooperative efforts of physiologists, otologists, physicists, neurologists, histologists and special space-research teams. This could lead towards a better knowledge of labyrinthine problems.

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*[1] Benson was of the opinion that the membranous canals could be deformed under the influence of linear acceleration - because of the s.g. difference between endo - and perilymph.

*[2] In the vertigo centre of the Wilhelmina Gasthuis the function of the otoliths is tested separately during routine vestibular investigations.

Because electronystagmography is one of our main diagnostic tools in the research of vestibular responses, it is important to understand the basic conceptions of its mechanism. The first attempts to record eye movements were as early as 1891 by Berlin, Högyes (1899), Buys (1909), Ohm (1914), Struycken (1918), Dohlman (1925) and Kuilman (1931). They used photography and mechanical devices.

In 1922 some early publications appeared on electronystagmography by Schott. Electronystagmography is a far more economical and easier method. The principle of the method is that there exists a constant retina-corneal potential difference, which was described by du Bois-Reymond (1849). The retina is charged negative and the cornea positive. As a matter of fact this potential difference can be regarded as a dipole situated in a fixed position with respect to the eye (Perlman 1939). Any movement of the eye between the two electrodes on the skin give a change in the recorded voltage.

In our research it is important to record the exact excursions of the eye as a function of time. Here we meet with a problem, which is: the choice between an A.C. or D.C. type amplifier. Although the D.C. type gives a more exact reproduction of eyeposition, it is not so easy to handle as an A.C. amplifier (Philipszoon and Jongkees 1964). With an A.C. amplifier the deviation caused by a sudden change of the input signal drifts back to the equilibrium value in a period depending upon the so-called time constant. On the other hand, the recovery time of the amplifier is short enough to avoid difficulties due to a slow drift from the iso-electric line. An A.C. amplifier thus measures alterations of the signals without the D.C. components and a D.C. amplifier measures both the changes and the D.C. components of the signal. Furthermore, only the changes of potentials between the two electrodes are recorded. Rotatory movements about a frontal axis are not recorded by electronystagmography (Hamersma 1957), because the eyes then rotate about their electrical axis and the axis of the dipole does not move with respect to the electrodes. Second, any movement of the electrodes or the skin in which they are attached can lead to sham effects in the recordings, e.g. eyelid-tremours may simulate nystagmus.

Although we are fully aware of the possible influence of visual fixation on eye movements (if they are directly observed Hamersma 1957), it still remains important to confirm the mingographic recording by means of direct observation. In some instances we noticed that the eyes even move in opposite direction or independently of one another and that nystagmus can be limited to one eye. Bos (1962) reported the same phenomena (Bos, et al 1963) and Jongkees and Philipszoon (1964).

Electronics

The electronic devices are important for our recording technique of the eye movements as well as for provoking the desired stimuli causing the eye movements. For a general survey we summarized our recording system in a block diagram (Fig. 1).

As electrodes we used two subcutaneous hypodermic needles per eye and fixed them with elastoplast in order to exclude movement artefacts. The third electrode was placed in the centre of the forehead and was connected to the ground. The electrodes were so arranged that the recordings of both eyes deviated to the same side on the nystagmogram. The exact distance of the electrodes to the brim of the eyelids has no practical influence on the eye recordings (Bos 1962, Jongkees and Philipszoon 1964). We also tried aligator clips for electrodes, which gave the same results and were easier to apply. The input signals to the amplifiers were fed either directly via copper sliding rings or by telemetry (type T.E. 2 Ahrend van Gogh). Both types of signal relay were used in different experiments. We used an eightchannel Elema E.M. 81 recorder with pre-amplifiers type E.M.T. 12. The sensitivity of the pre-amplifier can vary between 20-2000 μ V/cm recording in seven steps. Usually our range was between 500-1000 μ V/cm.

The time in seconds and the position of the vertical as well as the horizontal turntable are recorded on the paper. On our request the time constant of the amplifier was modified to approximately 10 sec. by the factory. This means that when a step function is applied to the input of the amplifier, after a period of 10 sec. the output has decreased to $\frac{1}{e} = 37\%$ of the original value. The longer the time constant, the slower the oscillating signal that can be recorded. Unfortunately this is accompanied by an increase in noise and drift. A compromise for our use is 10 sec. This is also suitable as we shall see, for recording responses of barbecue-rotation experiments.

Mechanical devices

The apparatus used in our experiments was constructed in the clinic's own workshop. The mechanical turntable to induce the various stimuli such as the

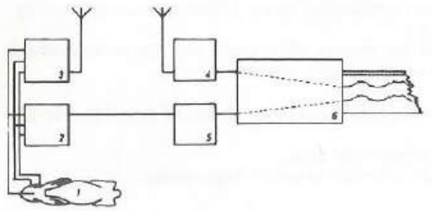

Fig. 1.

Block scheme of our recording system.

1. Test animal.
2. Copper sliding rings.
3. Telemetry transmitter (type T.E. 2)
4. Telemetry receiver (type T.E. 2)
5. Pre-amplifier E.M.T. 12.
6. Recorder E.M. 81.

barbecue rotation and the coriolis force was devided into two parts (fig. 2). This set up was controlled from a room nextdoor. The room which housed the rotation table could be darkened. By means of an "aerial indicator", which is a magnetic follower system, the angular position of the basic turntable could be noted. The electronic control for rotation table 1 (rotating about a vertical axis) could be programmed to produce the following stimuli: a constant acceleration and deceleration, a constant angular speed, a sinusoidal stimulus and a damped sinus (an electronic torsion swing) as explained in the legend to fig. 3.

The barbecue rotation table 2 (rotating about a horizontal axis) can be adjusted to rotate with various angular velocities at values ranging between 0.7 40 sec./rotation. Turntables 1 and 2 can be operated simultaneously to generate combined rotatory movements, amongst others, coriolis accelerations. By means of a counter weight the static balance of the barbecue turntable was assured, whilst the kinetic balance was checked by means of a stroboscope with the animal fixed in position and the rotation table in motion. This was done to prevent the generation of nystagmus provoked by undesired accelerations (and decelerations) during the phase of constant barbecue rotation. The rabbit-head holder we used is an improved model of the head-mouth clamp devised by Hallpike (1953).

Instead of using a mouth-bit between the teeth to stabilize the head, we used a bugle which tightly fitted over mouth and nose and was then firmly fixed to a steelbar (see fig. 2 no. 8) fixed onto the rotation table or operation table.

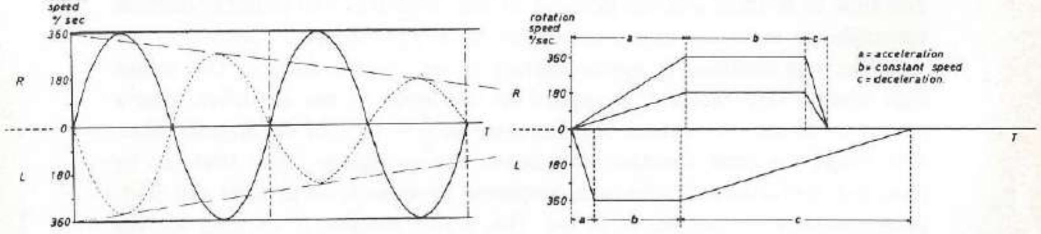

Fig. 3.

A B

Stimulus variations of the basic turn table.

A. The sinus represents the sinusoidal angular velocity of the basic turn table. It is produced by a Hewlett Packard low-frequency generator. It can be used in two different ways:

1) The continuous sinus curve represents a normal oscillating sinus. The frequency and amplitude can be changed.

2) The dotted "sinus" represents a damped oscillating sinus. (Eletronic torsion swing which imitates the mechanical torsion swing.)

The decrease of the amplitude is achieved by means of a small electric motor which linearly decreases the output signal of the low-frequency generator.

B. The linear lines represent the acceleration (a), a constant phase of rotation (b) and deceleration (c).

R = clockwise, L = counter clockwise rotation of the table.

In both figures the vertical axis represents the angular speed in degrees/sec.

On the horizontal line time is indicated.

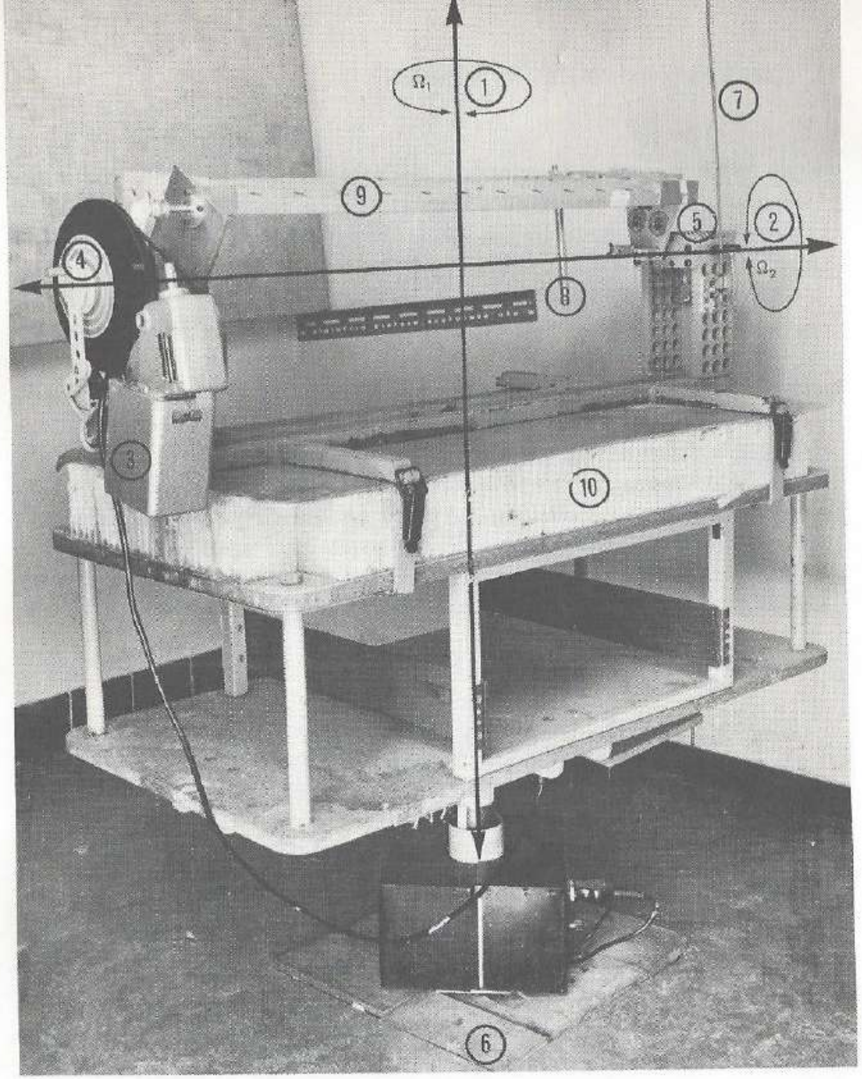

Fig. 2.

The turntable to provoke the various stimuli:

1) Vertical rotation axis. (Ω_1).
2) Horizontal rotation axis. (Ω_2).
3) Adjustable motor for the rotation of the barbecue-rotation table.
4) Stroboscope.
5) Copper sliding rings for the horizontal axial rotation.
6) Copper sliding rings for the horizontal and vertical rotation.
7) Antenna for the telemetry transmitter.
8) Rod for fixing the head-mouth clamp.
9) Horizontal rotation table.
10) Vertical rotation table.

1. CALIBRATION OF EYE MOVEMENTS

When nystagmography is performed, it is necessary to calibrate the eye movements in relation to the recorded responses. In human beings it is easy to calibrate the eye movements by just asking the patient to look alternately at two fixed points. This is not possible in rabbits. By passively moving the rabbit's eye between two fixed points, it is possible by measuring the amplitude of the curve on the recording to calibrate the input signal to the amplified recordings (Philipszoon 1959).

For this purpose we fixed the rabbit in a head-mouth clamp, while the electrodes were placed for horizontal and vertical recordings. Subcutaneous needle electrodes as well as aligator clips were used with identical results. Both the direct method of signal relay via copper sliding rings and cables and the telemetric system were coupled parallel to the same electrodes. In such a way we could also calibrate and compare the two methods of signal relay to the same input signal. After the cornea was cocainized, a thread was sutured into the cornea. Via a small pully one end of the thread was led to a counter weight, whilst the other end was moved over a constant distance, which in our case was 1 mm. By moving the eye over 1 mm we caused an upward or downward deflexion (depending on the arrangement of the electrodes) on the nystagmogram and when the counter weight pulled it back into position it caused a downward deflexion.

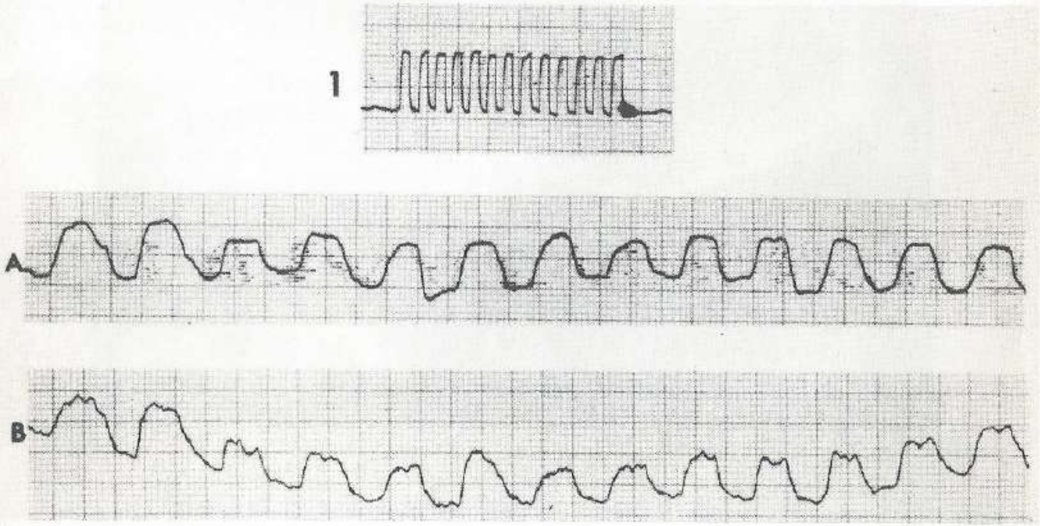

Fig. 4

Calibration of eye movements.

1) Amplification of the amplifier adjusted to represent 500 μ V as 1cm. on the vertical axis.
A) Direct relay recording.
B) Telemetry recording.
A. and B. were calibrated to give the same amplitude to an absolute eye movement of 1 mm.

We noticed that by moving the eye over 1 mm a deflexion of 1.3 cm on the recording resulted, whilst the amplification was adjusted to represent 500 μ V as 1 cm (Fig. 4). This means that at this amplification an eye movement is amplified 1:13 on the recording.

2. IDENTIFICATION OF NYSTAGMUS

Socrates stated that one should define key words in an argument. In our work the concept of nystagmus is of paramount importance. The word nystagmus originates from the Greek word "Nystazein", which means to nod. The definition of nystagmus is fairly broad and is amongst others described as eyeball convulsions with military regularity*[1], eye tremours*[2] or according to Dorlands Medical Dictionary: "an involuntary rapid movement of the eyeball. In our work we regard nystagmus as a rhythmic eye movement with a slow and a fast phase. Hence nystagmus in our opinion always has two components, these merit separate descriptions.

We shall outline what we consider as nystagmus with a few recordings. When

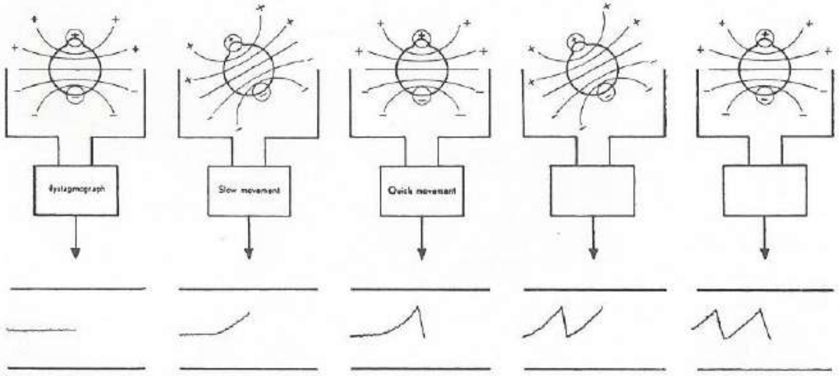

Fig. 5

Recording of Nystagmus.
The slow phase is directed upwards and the fast phase downwards.

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*[1] Pinkhof Geneeskundig Woordenboek.
*[2] Schuurmans Stekhoven Geneeskundig Woordenboek.

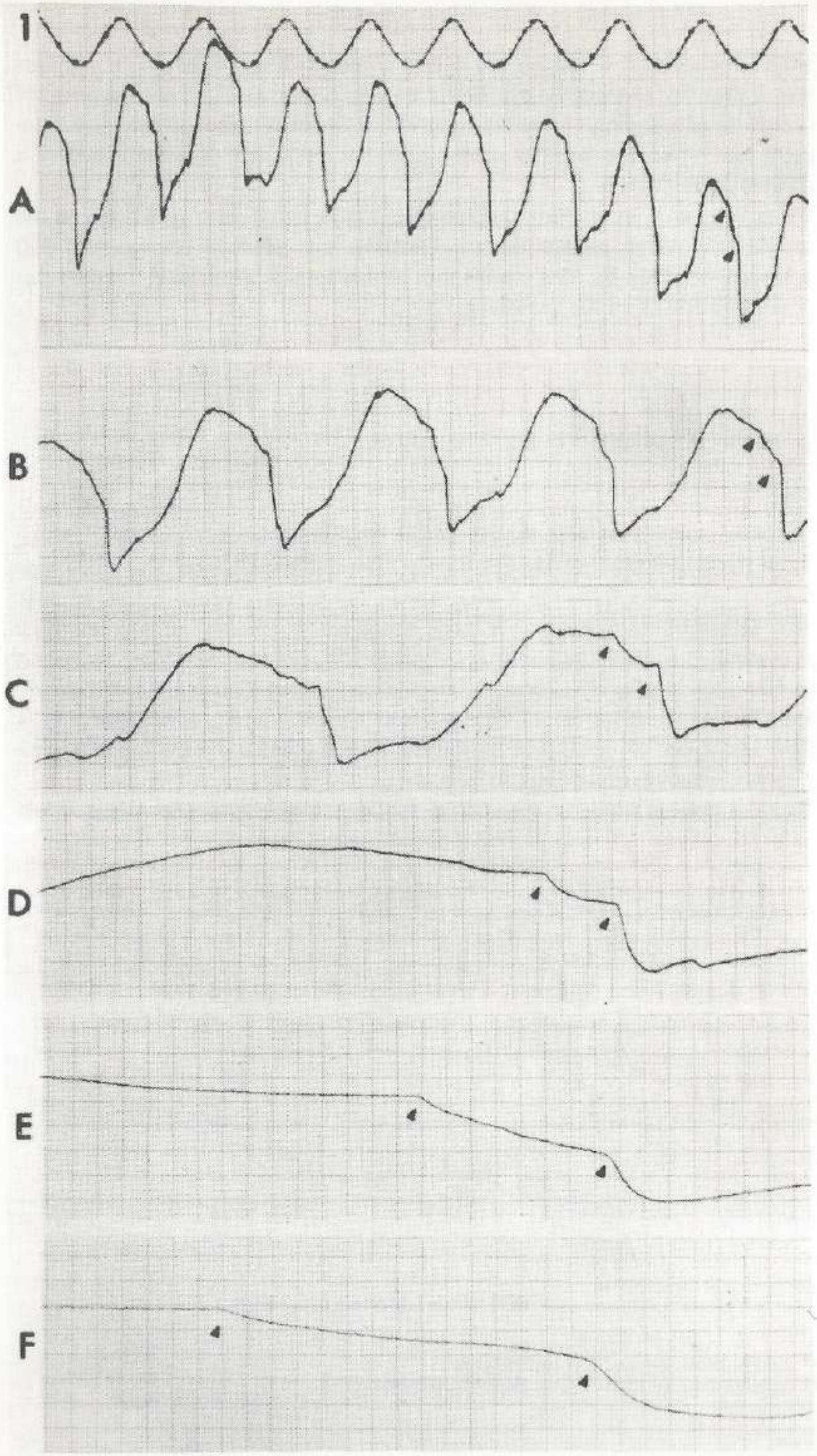

Fig. 6 (see left page).

Identification of nystagmus

The upper recording demonstrates the same barbecue response recorded with different paper speeds.

1. Barbecue rotation.
A. Paper speed .25 cm /sec.
B. Paper speed .5 cm /sec.
C. Paper speed 1 cm /sec.
D. Paper speed 2,5 cm /sec.
E. Paper speed 5 cm /sec.
F. Paper speed 10 cm /sec.

a pure nystagmus is recorded mingographically, it is represented with a slow and a fast phase. At normal paperspeeds (1 cm/sec.) the angle between the slow and the fast phase is usually not more than a right angle as demonstrated in fig. 5. But when the nystagmus is superimposed on an already present eye movement, the angle may exceed a right angle. If we increase the paper speed, a clearer image of the responses is obtained. The examples in fig. 6 demonstrate the same eye movement recorded with different paper speeds. In the upper recording the nystagmus is hardly recognizable and it appears that the angle between the two components is bigger than 90°. When the paper speed is increased, the actual angle comes to light, which is demonstrated on the lowest recording. It also shows that a concealed nystagmus is sometimes brought to light on faster paper-speed recordings.

In fig. 7 the upper curve is a sinus and represents either a baseline or the compensatory eye deviation (as provoked by the e.g. a barbecue rotation). To

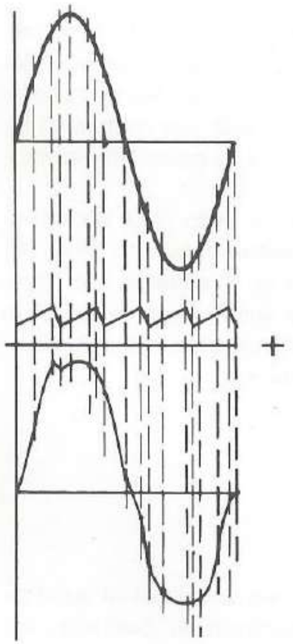

Fig. 7

Absorption of nystagmus beats superimposed on a sinusoidal curve.

The upper sinus curve represents the eye movement. The saccadic figure represents nystagmus beats and the lower curve is the summation of the upper two curves. It demonstrates the absorbtion of five unilateral nystagmus beats of which only one is recognizable as a nystagmus beat in the latter case.

this curve is added a pure rhythmic nystagmus and the lower curve is the final figure when both responses are added together. One notices how the slow and fast phases are indistinguishable at first and how with greater paper speeds, the angle between the slow and fast phase can show up as bigger than 90°. The above considerations demonstrate the necessity of refined electronic instruments for the study of labyrinth physiology and also the value of electronystagmography in our intended study of the responses caused by barbecue rotation.

3. BASIC VIEWS OF THE BARBECUE RESPONSES

Although electronystagmography provides the possibility of a more accurate study of labyrinth responses it is preferable that a nystagmographical recording is accompanied by direct observation with good illumination. This is a precaution to evade errors. One reason is that a rotatory eye movement about the eye axis is not recorded by conventional electronystagmographical techniques (Hamersma 1957, Jongkees and Philipszoon 1964, Jongkees 1966). For the basic observation of the reaction to barbecue rotation, we always looked first at the eyes of the animals.

The movements of the eyes in twenty animals were recorded in order to obtain more accurate details.

The rabbits were firmly fixed to the barbecue rotation table, because any sliding movement of the body might interfere with the kinetic balance of the turntable. This might provoke an unwanted angular-acceleration nystagmus. As stated earlier, the static balance of the rotation table was established by counter weights, and the kinetic balance was checked by means of a stroboscope attached to it.

The head-mouth clamp was fixed in such a position as to place the lateral semicircular canals in a horizontal plane; the occipito-frontal axis tilted 30° forwards. The rotation speed was one revolution in 10 seconds. The hypodermic needle electrodes as proposed by Jongkees and Philipszoon (1964) in their monograph "Electronystagmography" and aligator clips were compared. Horizontal as well as vertical leads were used for recording.

Direct visual observation of the eye movements

During barbecue rotation at a constant speed an eye movement of continuously changing direction was noticed in all the tested animals. Both eyes participated equally in these movements. This lasted as long as the barbecue rotation was applied. The position of the eye axis changed rhythmically in accordance with the position of the turntable as it rotated through 360° (Fernandez 1967).

Maximal eye deviation was observed when the rabbit occupied one of the two lateral positions. These are the turntable positions 90° or 270°. As soon as the rotation commenced, the eyes deviated in a direction opposite to that of the turntable motion. When the turntable had covered an angle of about 45°, the eyes occupied a maximally deviated position. This could be judged by the amount of white conjunctiva exposed between pupil and rim of the eyelids. The position of the eyes was maintained until the rabbit reached its side position (turntable position 90°). When the rotation proceeded beyond 90°, the eyes abandoned this position and started to deviate in the same direction as the turntable rotation.

The eyes switched to a neutral position before the 180° turntable position was reached and appeared to even overshoot the zero position. There after the eyes continued to deviate in the direction of the rotation of the table until at 270° where they reached an exact mirror image of the eye position at 90°. From this position on the eyes gradually came back to the neutral position. This deviation was in a direction opposite to that of the turntable. The neutral eye position was reached before the animal was exactly in its prone position, and at the 360°/0° turntable position the eyes were already deviated from the horizontal position on their course to the following rotation cycle. The eye deviations were nearly vertically directed, and had only a small horizontal component. For that reason we used vertical as well as horizontal leads.

Conclusion

During rotation about a horizontal axis, rabbits, when visually observed, show a continuously changing eye deviation which lasts as long as the barbecue rotation is applied. The maximal eye deviation occurs when the rabbit occupies a side position. The direction of the eye deviation alters itself rhythmically in relation to the barbecue rotation. The eye deviation is opposite in direction to the turntable rotation, when the rabbit is rotated from one side position via the prone position to the other side position.

From the side position via the supine position the eye deviation is in the same direction as the turntable motion.

Electronystagmographic recording of the slow-phase eye movements provoked by barbecue rotation

The general pattern of slow phase eye movements in the dark was the same as when visually observed in an illuminated surrounding.

The eye deviation recording varies sinusoidally in an upward and downward deflexion in accordance with the turntable position. Maximal eye deviations were noticed when the rabbit occupied a lateral position, minimal deviation occurred when the rabbit was approximately in a prone or supine position.

The amplitude of these eye movements was different for the horizontal and vertical leads. Vertical recordings were always of a larger amplitude than the horizontal ones (mean values 5.4 cm and 1.9 cm respectively).

The amplitude also differed between left and right eyes depending on whether the turntable motion was clockwise or counter-clockwise. If the rotation was clockwise (as seen from the animal), the left eye showed a smaller eye deviation than the right eye. When the rotation was inverted, so were the amplitudes (fig. 31 A, B. fig. 23 A, B, C, D).

This was a constant finding, especially on the vertical leads. The mean recorded amplitude for a clockwise rotation measured 5.6 cm (±1.3) for the right eye and 5.2 cm (±1.5) for the left eye on the vertical leads.

The horizontal leads then recorded 1.8 (±0.3) for the right and 2.1 cm (±0.6) for the left eye. It thus appears that the axis of the eye deviation was obliquely directed in relation to the horizontal and vertical leads.

If the output recording is closely compared with the input stimulus, it appears that there exists a slight but constant phase difference between the two eyes. This could be corroborated when the clockwise and counter-clockwise recordings were compared.*

The right eye anticipated the left during a clockwise (cw) rotation. The left eye anticipated the right if the rotation was inverted.

This anticipation factor could not be measured quantitavely since the amplifier was of the A.C. type and hence does not reproduce the exact mid position of the eye. The effect was qualitatively confirmed in many repetitions. The eye recording with the higher amplitude always was the anticipator. The phase anticipation varied between 0.5 - 1.0 sec.

In addition to the direct observations it can be concluded:

There exists an anticipation between the input stimulus and the eye-deviation recording. The amplitude of the eye deviation varies between the two eyes in accordance with the direction of the turntable motion.

Discussion of the eye deviation found during a constant barbecue rotation

Labyrinthine reflexes can be divided into those provoked by angular accelerations and linear accelerations (Mach 1875 and Breuer 1874, 1891). The semicircular canals and otoliths, respectively are stimulated by these stimuli (Jongkees 1944, Groen and Jongkees 1946, Philipszoon 1959 and 1962, Jongkees and Philipszoon 1964). Nowadays it is a matter of common knowledge that otoliths stimulated by a linear acceleration lead to compensatory eye movements. The barbecue rotation is not a linear acceleration stimulus per se, but a uniform rotatory movement in the field of gravity leading to a rhythmic reorientation to gravity (Guedry 1964). The fact that a varying inclination angle to the vertical acts as an otolithic stimulation, was clearly demonstrated by Löwenstein and Roberts (1949) and by Beerens (1967).

For these experiments the former used isolated labyrinth preparations of the thornback ray and the latter the utricular nerve in anaesthetized cats. In both studies impulses derived from the otolith organs were recorded at various inclinations. Löwenstein recorded maximal activity when the preparation was perpendicular to the horizontal plane. This corresponds to the eye deviation provoked by the barbecue rotation. A maximal eye deviation was recorded when the rabbits occupied a side position. It appears that the eye deviation is a sinus-like function of the inclination angle. The measurements from the isolated nerve did not demonstrate any difference of the eye-deviation amplitude, if the direction was inverted from clockwise to counter-clockwise. The number of impulses appeared to be only a function of the instantaneous inclination.

In the light of the above discussion one would be inclined to consider the eye movement provoked by the barbecue rotation as an otolithic response. The action of linear accelerations on the labyrinth has to be sought in the otoliths and not in the canals (see lit. rev.).

Yet similar eye deviations can be evoked by a torsion swing (see lit. rev.). Fig. 8 demonstrates a recording of the movements of the eye of both a human and a rabbit on the torsion swing.

A rhythmic eye deviation is demonstrated, with the same period as the sinusoidal stimulation. This was also the case in the barbecue rotation. No otolith stimulation is provoked by the torsion swing, here the eye deviation is of cupular origin. Ledoux (1950) relayed impulses from the nerve from the lateral semicircular canal when stimulat by a linear acceleration (centrifugal force). Suzuki, et al (1964) even provoked compensatory eye movements induced by single-fibre stimulation of each separate canal. It follows that in our case a rhythmic eye deviation can be either cupular or of otolithic origin. If the eye deviation provoked by the barbecue rotation is of cupular origin, then the cupula must have a larger or a smaller specific gravity (s.g.) than the surrounding endolymph (see lit. rev.).

Another possibility is that there exists a difference between the s.g.'s of endolymph and perilymph. Dähnhardt (1869) reported that the "solid constituence" of endolymph and perilymph were 1.5 and 2.1%, respectively. More recent work from Kaieda in the shark (1930) indicates an s.g. ratio 1.0204 to 1.0200 between endolymph and perilymph. During a barbecue rotation a continuous redistribution of fluids in the canals might occur as long as the rota-

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*It might be explained as a kind of cybernetic function of the central nervous system to anticipate the horizontal plane during a barbecue rotation (Mayne 1965).

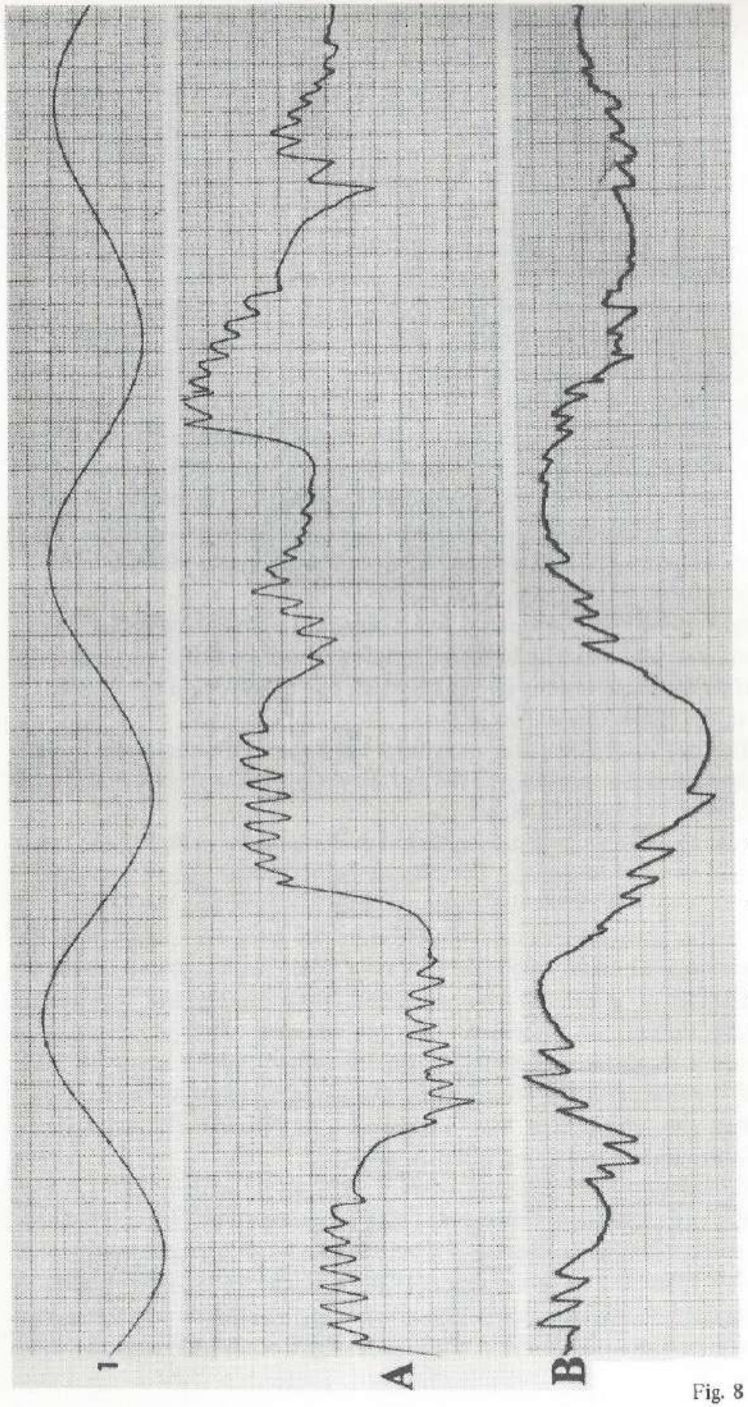

Fig. 8

Compensatory eye movements provoked by a torsion swing
I = Torsion-swing recording.
A = Cupular responses of a rabbit.
B = Cupular responses of a human.

tion persists. This would then produce a pressure difference across the cupula which would be deflected, and could generate an eye deviation. The eye deviation would, in this conception, be evoked by the cupula as in the case of the torsion swing.

Benson and Bodin (1965), reported "anti-compensatory" eye movements "at the commencement or cessation of a barbecue rotation". They could not state with confidence that in man any oscillating eye deviation persisted during the period of constant rotation. Viewing the recordings puplished by Guedry no constant eye oscillations could be noticed either. (Guedry 1964).

Although it is highly probable that the eye movements in the case of the barbecue rotation is of otolithic origin, this view must be regarded with some reserve.

Recording of the total nystagmus during constant barbecue rotation

As soon as the barbecue rotation commences, a nystagmus devellops. The nystagmus during the first few rotation cycles may be regarded as provoked by acceleration. After the acceleration ceases, a sustained per-rotational nystagmus is found. That means: in addition to the aforementioned slow phase eye movements there appeared quick jerks of the eye. Of the 20 tested rabbits, 18 showed this complex response. On two rabbits, only an eye deviation without nystagmus was noticed. The quick jerks showed a preference to appear at the moments where the eye deviation is maximal. In addition their amplitudes were largest around the region of maximal deviation. The amplitudes of the nystagmus beats in our experiments were bigger on the horizontal leads than the vertical ones (as judged by the amplitude of the quick phase).

McCabe (1964) also found that nystagmus appeared within the period of "the greatest build up of gravity".

The amplitude of the quick phase was measured on the horizontal recordings. The right eye gave a mean value of 7.5 mm, the left eye was 8 mm (calibration was $500\ \mu V = 1$ cm). This holds for a clockwise rotation.

McCabe (1964), Benson and Bodin (1965, 1966), Niven, et al (1966) and Benson (1962, 67), only found a horizontal nystagmus. A vertical nystagmus was not mentioned.

The number of beats per cycle also varied. In some cycles the nystagmus even disappeared. The disappearance of nystagmus during certian cycles of stimulation has also been described by McCabe (1964). (see lit. rev.).

The mean amount of beats counted 3.6 for the right eye and 4.6 for the left eye. This was measured at a barbecue-rotation speed of 36°/sec. The reverse appeared for rotation in the opposite direction.

The distribution of beats per cycle was irregular. The beats occurred around the crest of the eye deviation. Very few beats were noticed between the turntable positions of 135°-170°, this being the position in which the eye deviation was minimal.

The direction of the fast phase of the nystagmus was the same as the angular motion, which implies that it is opposite in direction to the slow phase eye deviation. Of the 18 rabbits that showed a nystagmus only 3% of the beats for the right eye and 2% for the left eye were in the same direction as the eye deviation. This occurred between the turntable positions 170°-125°. Thus, the nystagmus occurred practically in one direction during the entire rotation. Most of the investigators in this field found the same (see lit. rev.).

Observing the curves published by Jongkees and Philipszoon (1961 and 1962), Philipszoon (1962), Bos, et al (1962), we notice that the nystagmus is in one direction as well. These authors used linear accelerations to stimulate the labyrinth.

Niven et al (1966), described a nystagmus in accordance with the direction of the acting linear acceleration. We also tested some human subjects on the parallel swing, while they were lying on their side and looking to either the left or the right. We noticed a predominantly unilateral nystagmus during an acceleration in one direction. If the acceleration inverts so does the nystagmus (fig. 8).

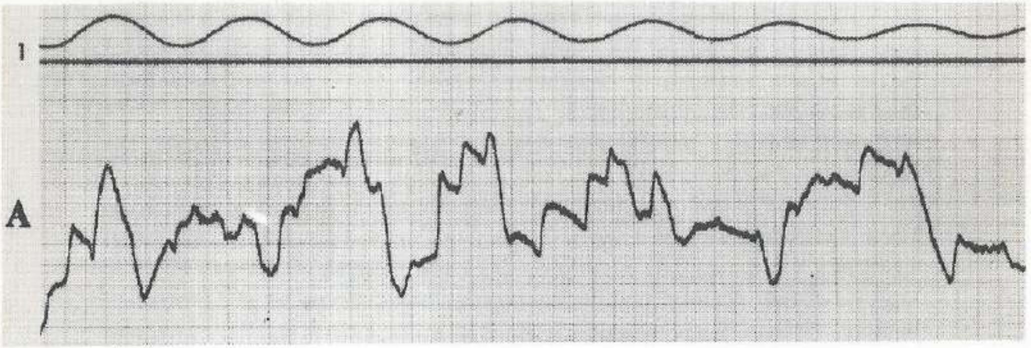

Fig. 8a

Responses provoked by a parallel swing in a human. The person was lying on his left side
1 = parallel swing.
A = nystagmus.

Discussion on the nystagmus beats during the phase of constant barbecue rotation

During our experiments we constantly recorded larger amplitudes of the nystagmus beats on the horizontal than on the vertical leads. In fact the nystagmus was diagonal in direction and it underwent cyclical modulation of intensity. Fernandez (Collegium O.R.L.A.S. Chicago 1967) reported a special type of rotatory nystagmus about a central axis provoked by a coriolis stimulus in alabyrinthine cats. He used photometry to record the eye movements and is thus sure of the actual pathway of the eyes. This observation concerning nystagmus of which the direction rotates about a central axis is partially applicable to the barbecue nystagmus. It could be possible that the nystagmus during a barbecue rotation varies in direction. This rotatory effect cannot be more than 45°, because the vertical lead always demonstrates a nystagmus of a smaller amplitude than the horizontal lead. Thus, some change of the direction of nystagmus might explain the cyclical modulating effect on the amplitude of the nystagmus.

If it were true that the barbecue nystagmus originates from an endolymphatic displacement and hence were of cupular origin then the nystagmus would be either rotational or vertical according to Ewald's law (which is, that eye movements are predominantly the plane of the stimulated canal). This is not what we found. It is thus highly probable that the otoliths and not the cupulae are responsible for this form of nystagmus when the animal is constantly reorientated with respect to the direction of gravity.

4. EFFECT OF VARYING THE ROTATION ANGLE

Introduction

If the canal system is regarded as being gravity sensitive, it should be possible to demonstrate a difference between the labyrinth responses of cupular origin at different angles of inclination or declination to gravity. For instance, a) the direction of nystagmus should change as the different canals (vertical and horizontal) are affected by the concomitant vertical gravity, and b) the responses of the labyrinth should be equal at + and - 45°* because in these two positions the canal system is identically oriented to gravity.

Execution

For this purpose we used 20 normal animals. The experiments were performed in the dark. At the beginnen of each experiment the animals were fixed on

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*+ 45° indicates that the head is upwards and - 45° that the head is downwards (see fig. 9).

the barbecue-rotation table with the head-mouth clamp so adjusted as to place the lateral semicircular canals in a horizontal plane. (The angle which the occipito-frontal plane of the skull makes with the horizontal plane was measured in dried rabbit skulls. The lateral canals as well as the anterior and posterior vertical canals were dissected around most of their circles with a burr under guidance of a microscope. We thus ensured that the lateral canal was really in a horizontal plane and that the vertical canals were co-planar with gravity). The rotation table was now switched on and brought quickly to a constant angular speed of about 36°/sec. The whole rotation table could now be slowly inclined and declined from the horizontal plane, so that eventually the axis of rotation was in a vertical plane (fig. 9). It implies that in extreme positions the animals rotated about a longitudinal vertical axis with either the head up or down. The eye movements were recorded at 0° (position 1 fig. 9. rotation axis in the horizontal plane) ±10°, ±45° (positions 2 and 3) and in both vertical positions (4 and 5) head up and down.

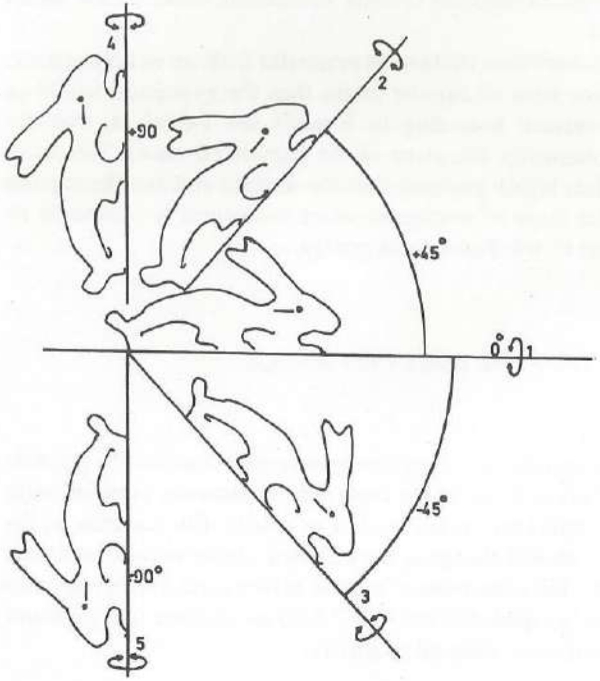


Fig. 9

The different positions of the axis of rotation.
1 = rotation about a horizontal axis.
2 = the axis of rotation is inclined +45° in relation to the horizontal plane.
3 = the axis of rotation is declined −45° in relation to the horizontal plane.
4 and 5 = vertical axial rotation; 4 = head up and 5 = head down.

Observations

Within the first 10° we noticed practically no change of the basic responses. The amplitude of the nystagmus as well as of the eye movements was unchanged. At +45° (head upwards) the amplitudes of the eye movements and nystagmus beats were markedly reduced. This was the case for both the horizontal and vertical leads. The nystagmus remained in the same direction on both leads.

When the axis of rotation was declined to −45° from the horizontal plane (head downwards), the recording of the vertical and horizontal leads differed as regards the amplitude of the eye deviation.

On the vertical lead it was noticed that the amplitude was reduced to approximately the same value as at +45°. On the horizontal lead the amplitude showed an increase above the value measured when the axis of rotation was in a horizontal plane. Although the amplitude of the eye movements is reduced when the axis of rotation is inclined to +45° the eye moves in the same direction (with respect to the animal) as in the horizontal-rotation case. When the axis of rotation is −45° the eye moves more in the plane of the horizontal leads than in that of the vertical ones (fig. 9a and fig. 10).

The nystagmus at −45° remained in one direction. It implies that whether the rotation axis is −45° or +45° the direction of the nystagmus remained fixed. We could not detect any shift of the phase of the eye deviation in relation to the input stimulus at the various rotation axes.

During constant rotation at ±90° compensatory eye movements and nystagmus on both leads are reduced to zero. During acceleration the nystagmus remained present when the axis of rotation was in a vertical plane.

The above results demonstrate:

1) The maximal amplitude of both compensatory eye deviation and nystagmus is recorded on the horizontal leads when the rotation axis is tilted −45° from the horizontal plane and on the vertical leads when the axis of rotation is in a horizontal plane. (fig. 10).
2) The nystagmus during the phase of constant rotation remains in the same direction disregarding the angle of the axis of rotation with respect to gravity.

Discussion

Let us again assume for a moment that the canals are gravity sensitive e.g. since the endolymph has a s.g. different from the perilymph. When the lateral

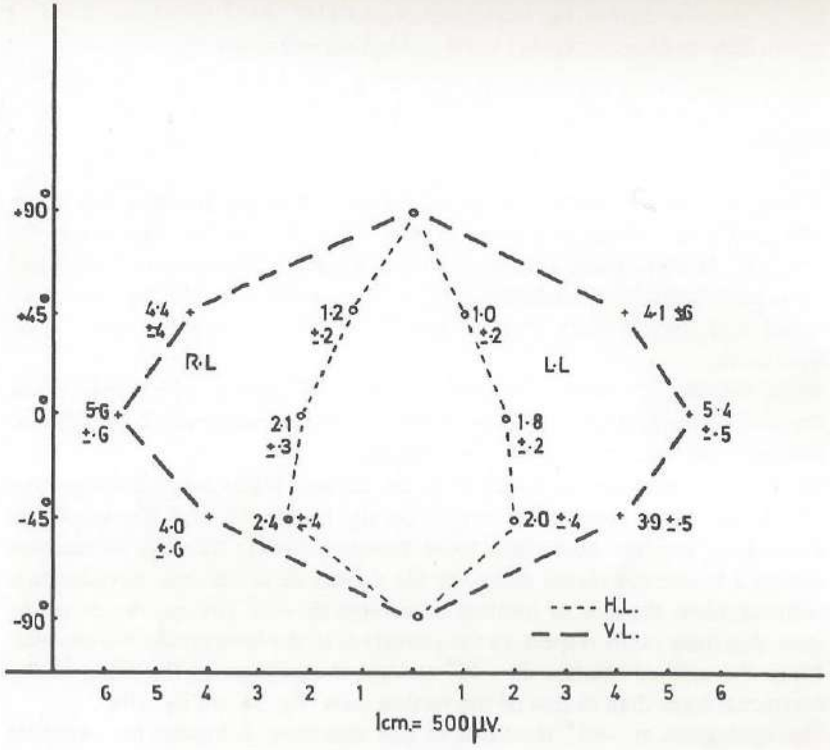


Fig. 9a.

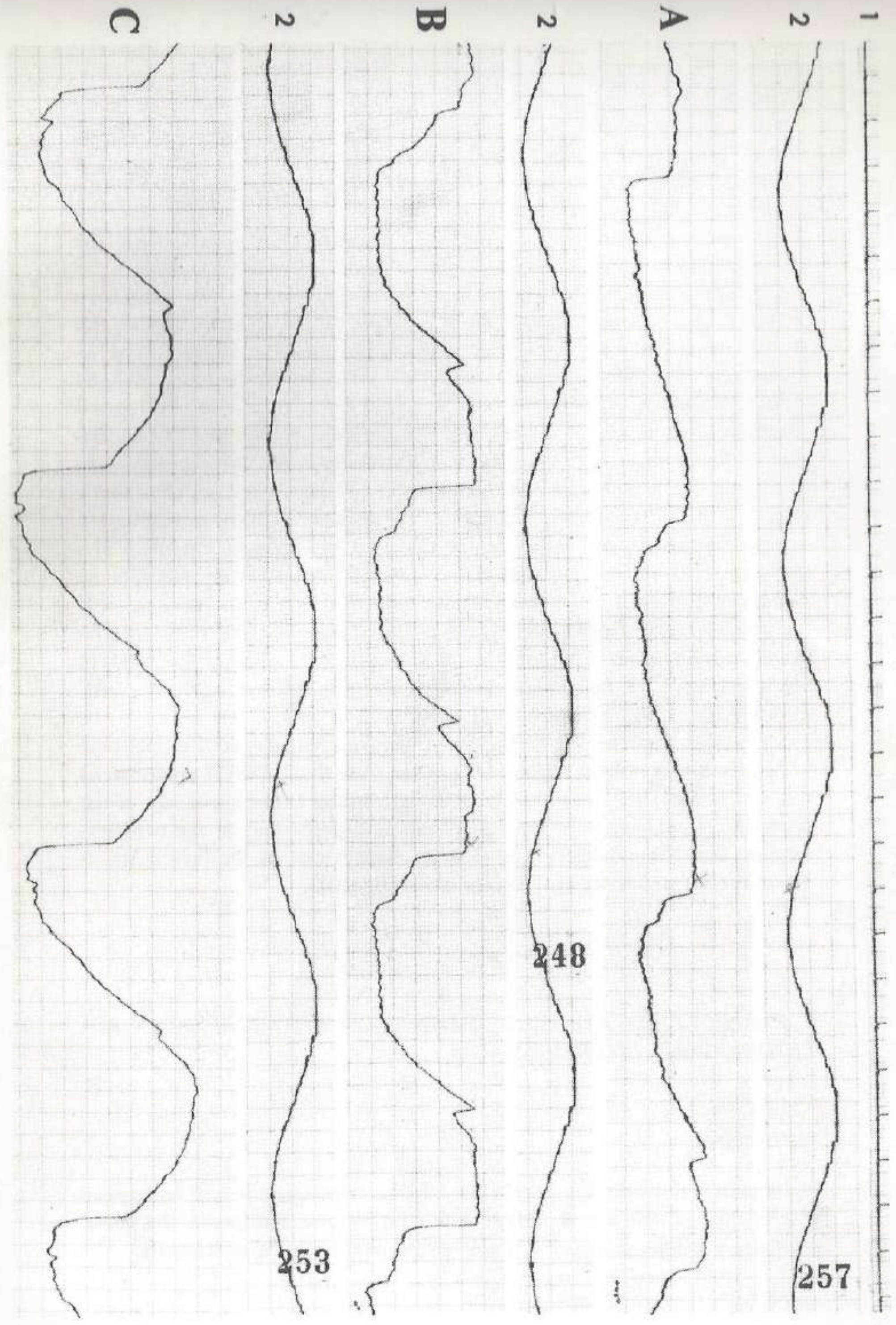
Graphic representation of the labyrinth responses at different angles of in- or declination from the horizontal plane.
Vertical axis represents the amount in degrees of the in or declination.
R.L. = right lead; L.L. = left lead.
V.L. = vertical lead; H.L. = horizontal lead.
The horizontal axis represents the labyrinth responses measured as a function of the eye deviation.
The formula $\sqrt{\frac{\left(\bar{x}^2\right) - \left(\bar{x}\right)^2}{N}}$ was used to calculate the spreading factor. Where x represents the individual responses and N the amount of animals which participated in the experiment (N = 10 rabbits for each lead).

Fig. 10 (see right page).

Labyrinth responses at different rotation angles (horizontal lead recordings).

1 = Time in seconds.
2 = Barbecue rotation.
A = rotation angle inclined +45° in relation to the horizon. (See fig. 9 - 2)
B = rotation angle in a horizontal plane. (See fig. 9 - 1)
C = rotation angle declined −45° in relation to the horizon. (See fig. 9 - 3)

The amplitude of the eye deviation is largest when the axis of rotation is −45°.



canals are placed horizontally, the vertical-canal system is co-planar to gravity and is in an optimal position to signal any changes in the direction of gravity. When the axis of rotation is directed at +45° or –45° with respect to the horizontal plane, the canals are in this respect identically positioned in relation to the direction of gravity. Then the recordings of the responses should be more or less the same in both positions. Though they may be somewhat reduced compared to the 0° position.

Experimentally, this proved not to be the case. There exist a difference on the horizontal lead responses between the + and –45° position. Also, if the canals were stimulated by gravity, then the direction of the nystagmus beats should change when gravity stimulates different canals. A rotation nystagmus is then expected. Our findings were that the direction of nystagmus remained constant since the direction of the nystagmus on the horizontal and vertical recordings did not change.

By direct observations we did not find rotation nystagmus either. Our conclusion is that both the compensatory eye deviations and the accompanying nystagmus beats during barbecue rotation at constant speed are of otolithic origin. A reason for the slight change of the plane of the slow compensatory eye movement at –45° could be the fact that the utricular macula is in a plane nearly parallel to the base of the skull (±10°), (James 1968), while the canals are situated at a 30° angle to the base. This means that at + or –45° the canals occupy the same position in relation to gravity, whilst the utricular macula is positioned differently at –45° and at +45°. This difference is in agreement with the increase of the labyrinth responses noticed on the horizontal lead when the axis of rotation is declined to –45°.

From the behaviour of the amplitude of the eye deviation and the amplitude of the quick phase of the nystagmus, one can state that these are proportional to one another. This is to some extent a contribution to our knowledge of the provocation mechanism of the fast phase. It suggests that in the constant-rotation case the amplitude of the slow phase is one of the factors which determine the amplitude of the quick phase (fig. 10).

5. BARBECUE ROTATION IN COMBINATION WITH SINUSOIDAL ROTATION ABOUT A VERTICAL AXIS

Introduction

Nystagmus is normally considered the cupular response provoked by angular acceleration. If the eye deviation was also a cupular response the phase should invert if the direction of acceleration about a vertical axis inverts.

In the light of the above basic principle we applied a combination of a barbecue rotation and a sinusoidally changing acceleration about a vertical axis; it should then be possible to analyse the difference between labyrinth responses of cupular or otolithic origin. In addition, this compound movement is three dimensional and hence will stimulate all three (six) cupulae and all the otoliths.

Execution

We conducted some experiments in rabbits in which a combination of two stimuli was applied to a pair of normal labyrinths - a basic constant rotation about a horizontal axis perturbed by a slow sinusoidal rotation (c.a. .02 Hz) about a vertical axis. It seems a very simple matter but the mathematical evaluation of the generated spacial vector is rather complicated.

The motive for choosing this seemingly extremely complicated stimulus was that it offers an easy method of measuring threshold values, because the perturbation (i.e.: the periodically changing vertical rotation), changes from zero to maximum and via zero to the opposite polarity.

Horizontal and vertical leads were used for recording. The experiments were performed in the dark. After the electrodes had been securely placed intradermally, the animals were fastened in such a position that the lateral semicircular canals were in a horizontal plane. After this, the barbecue rotation and then the vertical axial rotations were recorded separately; the combined stimulus of the barbecue and the vertical-axial rotations followed. For the sake of clarity the results are discussed with the aid of a few typical recordings.

In fig. 11 the acceleration about the vertical axis changes from clockwise to counter-clockwise. At zero acceleration only the weak nystagmus beats of the barbecue rotation are seen on top of the slow eye-movement recording. The beats become much larger when the acceleration increases to a maximum. In the two recordings for c.w. and c.c.w. vertical rotation the direction of these nystagmus beats is seen to be opposite to one another. The inversion of c.w. to c.c.w. suggests an inversion of the endolymphatic flow and an opposite deflection of the cupulae. One would expect the nystagmus direction to invert as well. What is interesting, though, is not that the nystagmus direction inverts, but that the rhythm and phase of the slow eye deviations stay constant. This can only be explained if one assumes that both types of slow eye movements viz: the slow phase during the acceleration and the eye movements due to re-oriëntation are generated by different sub-organs of the labyrinth, namely the canals and the otoliths respectively. We may assume that the interaction of two rotational movements results in a coriolis acceleration which acts on every particle i) of the otoliths and ii) of the canal fluids. We believe the second factor to be the most important one for reasons that will be given shortly. The inversion of the nystagmus direction is then wholly in accordance with

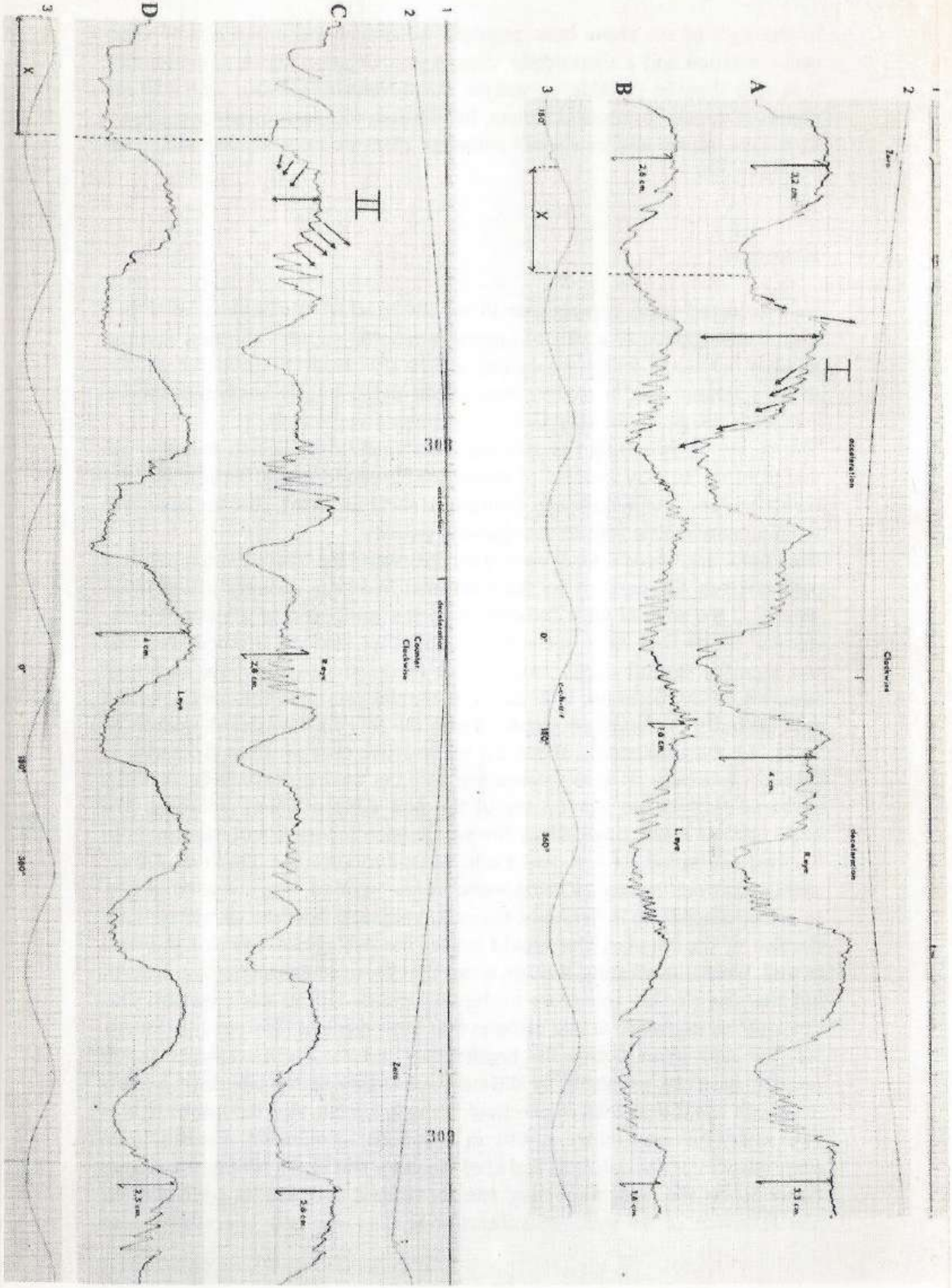


Fig. 11.

Eye movements of a rabbit during combined rotations about a horizontal and vertical axis.
1 = time in seconds; 2 = sinusoidal rotation (.02 Hz) about a vertical axis; 3 = barbecue rotation. A and C = movements of right eye; B and D = movements of left eye. I and II = two identical stimuli (x) caused by a constant barbecue rotation, but opposite vertical axial accelerations. In I the vertical acceleration is clockwise and in II counter-clockwise. The oblique arrows indicate the direction of the slow phase of the nystagmus, the vertical arrows the amplitude of the eye movements. In case I the slow phase is co-directional to the phase of the eye deviation and causes an increase of the eye-movement amplitude. In case II the slow phase direction is opposite to the eye movement and cause a reduction of the eye-movement amplitude.

our classic conception of labyrinthine physiology. The explanation that the rhythmic pattern of the eye deviations is not altered is that the otoliths are only stimulated by the reorientation to the direction of gravity and thus remain in phase with the barbecue rotation. The variation of rotatory movements about the vertical axis do not influence the linear receptors at all.

The proof that the centrifugal force evoked by the rotation about the vertical axis has no practical influence on the otoliths is demonstrated in fig. 12, where the vertical axial rotation is halted at the point of maximal angular stimulation (within three seconds, thus a period well below the 10 sec. time constant of our A.C. amplifier and the iso-electric line can be regarded as more or less accurate), and no slow eye deviation is apparent. Since any coriolis force is always smaller than the largest of the centrifugal forces the effect of coriolis forces on the otoliths is negligible.

Fernandez (1968) reported that in his animals which were subjected to a typical coriolis* stimulus, the same baseline was noticed with a D.C. amplifier, which agrees with our results.

We review the situation as follows:

1) The direction of the nystagmus beats is inverted by the change of the movement about the vertical axis from cw to ccw or v.v. because of the inversion of the coriolis force.
2) The eye deviation is not inverted since the coriolis force generated by the above mentioned movement is too small to change the direction of the gravity vector enough.
3) Although in this case the cupula system responds to the coriolis stimulation, the eye position does not. The various components of the movements are caused by two different sub-organs, the canals and the otoliths.

Another point of interest is the amplitude of the eye deviation per se. Regarding two comparable responses of the same eye at the same barbecue stimulus but with the difference that the perturbing rotation has changed from cw to ccw one notices that the amplitude in the former case is greater than that of the latter case. (fig. 11).

This can be explained as follows: In case I (cw) the direction of the slow

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*(see definition of coriolis stimulation).

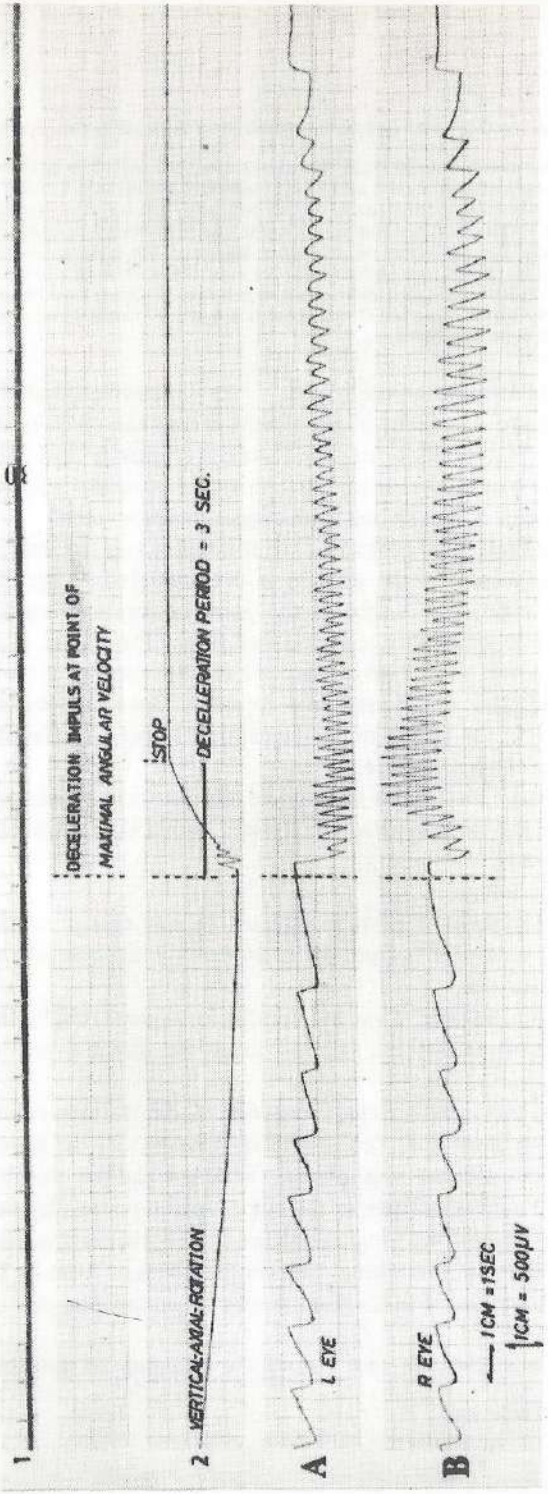

Fig. 12.

Stopping the movement about the vertical axis at the moment of maximum speed does not provoke a deviation of the average eye position.
1 = time in seconds.
2 = vertical axial rotation.
A = left eye; B=right eye.
This indicates that the centrifugal force has no action on the eye movements in this specific experiment.

phase of the nystagmus corresponds to the sense of the eye deviation and in case II (c.c.w.) the slow phase of the nystagmus is in the opposite direction. It appears that the slow phase of the nystagmus increases the amplitude of the compensatory eye deviation in one (case I) and reduces it in the other case (II). This observation leads to the following inferences:

a. It presents a further proof that the two different components are generated by two different sub-organs. It would seem improbable for the cupulae to be thrusted in one direction by the vertical rotation and yet at the same time, be it by some other mechanism (slosh), to be pushed in the opposite directions so as to generate the eye deviation.
b. Furthermore, it appears that the average amplitude of the amplitudes of I and II (which is 3 cm. in fig. 11) corresponds to the value which we recorded for a barbecue rotation without a concomitant rotation about a vertical axis. In somewhat different terms this can be described as an influence of the cupulae on otolith responses in the sense that the latter can be enhanced as well as suppressed. It thus appears that there exists a close co-ordination between the two sub-organs. The amount of the reciprocal influences depends on the combination of different accelerations, both rotatory and linear. Reviewing the literature there are a few authors who mention the influences of the otoliths on cupular responses. Guedry (1964) even states that the otoliths can maintain cupular functions. Although we found nowhere in literature that cupular responses can modify otoliths responses, this seems to be clearly demonstrated by our experiments.

In fig. 13 the effect of a faster angular speed of the barbecue rotation is recorded. As in the preceding case a sinusoidal vertical rotation was used. It appears that the amplitude of the eye deviation decreases while the intensity of the slow phase of the nystagmus increases, so much that it is hardly possible to distinguish the slow from the fast phase.

This again demonstrates the difference between the characteristics of the two different eye movements. The nystagmus is intensely stimulated by the increased barbecue speed, but the eye deviation has become less. Although this last phenomenon is not easily explained it suggests again that the two different types of eye movements are generated by two different sub-organs, both with their own characteristic.

6. EFFECTS OF DIFFERENT ANGULAR VELOCITIES ON BARBECUE RESPONSES

After having observed the basic responses of the barbecue rotation at 36°/sec. we investigated the effects of an increased angular speed. We tried to find out

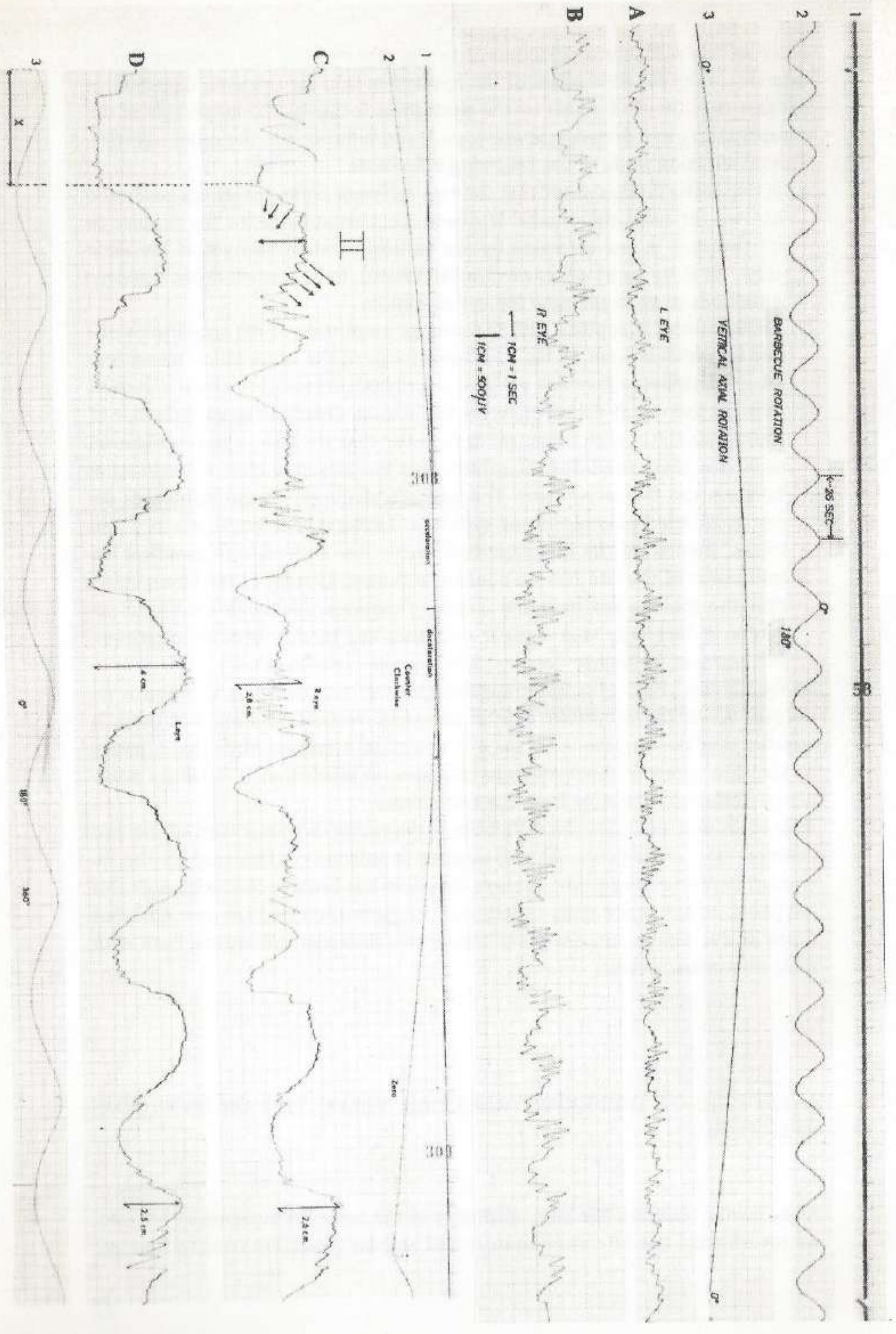

Fig. 13.

Eye movements provoked by the same stimuli as in Fig. 11 but for the rotation about a horizontal axis which is faster.
1 = time in seconds.
2 (upper) = barbecue rotation 2.5 sec./rotation (c.w.).
2 (lower) = vertical axial rotation (c.c.w.).
3 (upper) = vertical axial rotation (c.c.w.).
3 (lower) = barbecue rotation 9 sec./rotation (c.w.).
A and B (upper) = responses of left and right eye.
C and D (lower) = responses of left and right eye.
When the barbecue rotation speed increases the eye deviation amplitude decreases whilst the slow phase of the nystagmus increases.

whether a phase shift of the eye movement in relation to the input stimulus could be observed under extreme conditions.

Execution

We subjected 20 normal rabbits and 10 bilaterally a-labyrinthine rabbits to different angular speeds of 10 sec., 6 sec., 2.5 sec. and 1 sec. per rotation. All experiments were performed in a dark room. Paper speeds up to 5 cm./sec. were used in certain cases to detect any phase shift at greater angular speeds. The amplitudes of the eye deviation and of the nystagmus were measured as an indication of the function of the labyrinth at different angular velocities.

Observations

The a-labyrinthine rabbits did not demonstrate any response even at increased rotation speeds. This is highly suggestive that no mechanical forces, resulting from the change in gravity direction, cause eye movements.

All the normal rabbits in this series, except one, exhibited the same phenomenon, viz. in both the horizontal and vertical leads a marked reduction of the amplitude of the eye deviation occured. The responses were approximately inversely proportional to the angular speed. (fig. 15).

In one animal the amplitude of the eye deviation remained constant at all speeds.

Vertical-lead recordings still remained of higher intensity than the horizontal ones. We did not notice any phase shift in relation to the input stimulus; only at the extreme speed of one revolution in 0.7 sec. the eye movements lagged behind the input stimulus (in some animals as much as 90°). This was only noticed on the vertical leads, since the horizontal leads did not show any eye movements at this angular speed.

Benson and Bodin (1965) did not mention the behaviour of eye movements at faster angular speeds than 6 sec./rotation, in fact they were not able to measure eye movements in humans quantitatively.

The number of nystagmus beats at 1 sec./rotation reduced to about half the number measured at 10 sec/rotation (fig. 14). The average amplitude of the nystagmus beats remained about the same. This means that the ratio of the

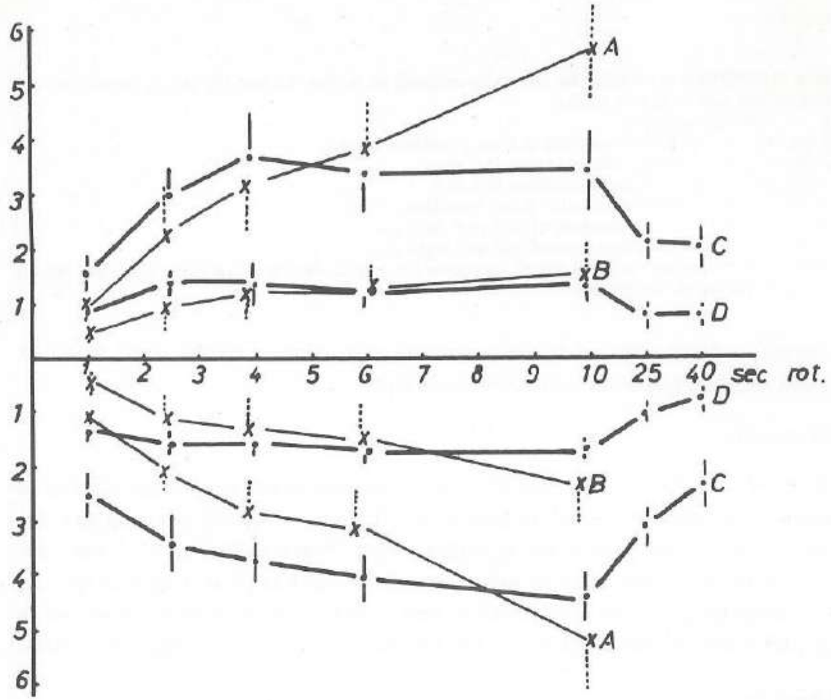

Fig. 14

The responses of the rabbit at various angular speeds.
A = Amplitude of the eye movements recorded from the vertical lead.
B = Amplitude of the eye movement recorded from the horizontal lead.
C = Amount of nystagmus beats.
D = Mean nystagmus intensity.
The vertical axis represents 500 μ V/cm. In the case of A, B, D and the mean amount of beats in the case of C.
The upper figure is the right eye responses and the lower is the left eye recordings.

amplitude of the eye deviation to the amplitude of the nystagmus decreases at faster speeds. At 1 sec./rotation the average nystagmus beat is approximately equal to the maximal eye deviation. (fig. 14).

The direction of the nystagmus remained constant at all angular speeds, except at the fastest rotation of 0.7 sec./rotation, where the nystagmus beats appeared to change rhythmically in direction, in relation to the change of the position of the labyrinth. Benson and Bodin (1965), Correia and Guedry (1966) also reported that the nystagmus direction change in direction at faster angular speeds.

We also counted the number of nystagmus beats at 25 sec. and 40 sec./rotation. Although this is beyond the limits of the time constant of our amplifier, it is still possible to detect nystagmus beats. At the slower angular speeds the

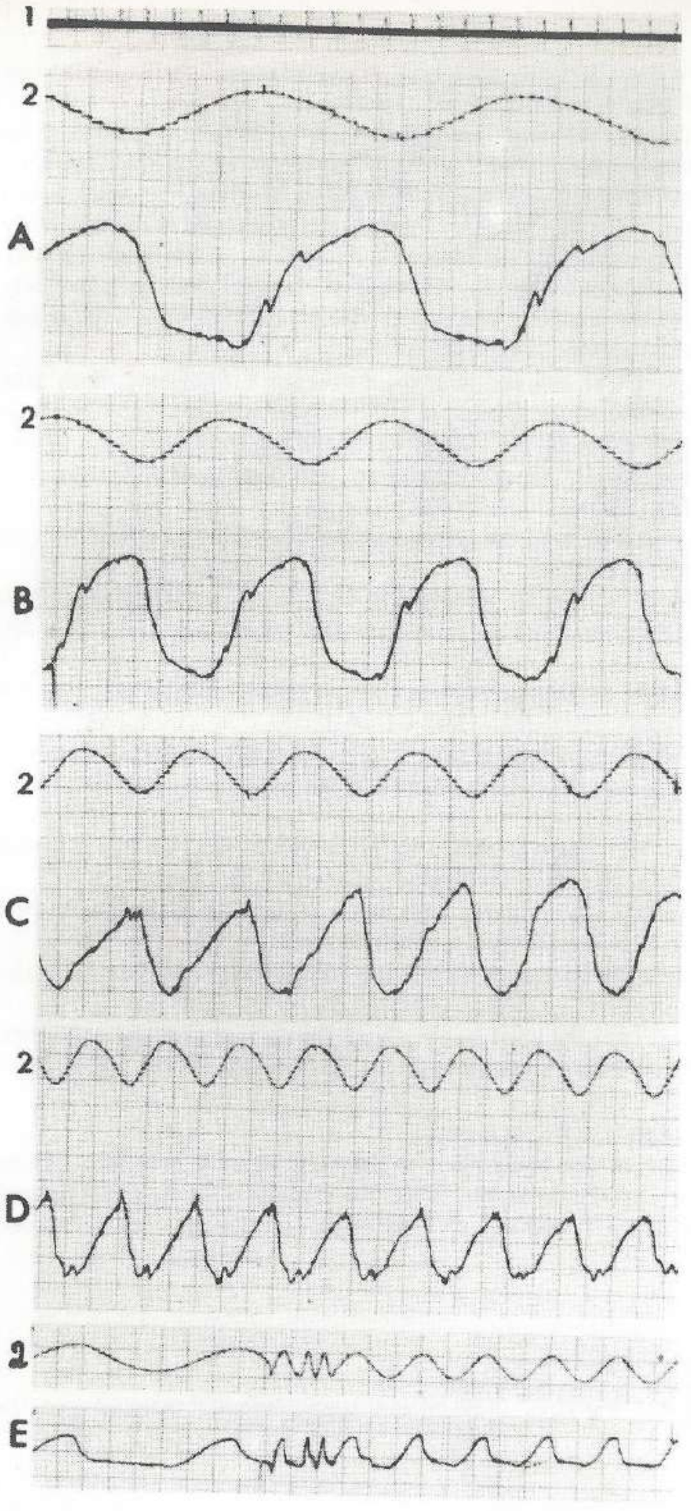

Fig. 15

Mingographic recordings of the eye movements at various angular speeds (vertical leads).
1 = time in seconds. 2 = barbecue rotation.

A = eye recording at 10 sec./rotation
B = eye recording at 6 sec./rotation
C = eye recording at 4 sec./rotation
D = eye recording at 2.5 sec./rotation
E = eye recording at 1 sec./rotation

The paperspeed in the latter case is 3 cm./sec. .5 cm./sec. and 1 cm./sec. in order to demonstrate the quick phase better.

number of nystagmus beats decreased to approximately half of the beats counted at an angular speed of 10 sec./rotation.

Benson and Bodin (1965) found an increase of the number of nystagmus beats when the barbecue speed varied from 36 sec. to 18 sec. and to 6 sec./rotation. This is in agreement with our experiments. When, however, the angular speed is increased beyond 6 sec./rotation, there results a decrease of the frequency of nystagmus to about half of the amount counted at 40 sec./rotation (fig. 14).

In order to understand why the amplitude of the eye deviation is inversely proportional to the angular speed, it is necessary to discuss some basic principles concerning the genesis of the phenomena.

Nystagmus consists of two components, a slow and a fast phase. Both have their own threshold values. (Jongkees and Philipszoon 1964). The slow phase can be provoked either by the cupular or by the otolithic system. (Jongkees and Philipszoon 1964). These principles are well demonstrated in a torsion-swing recording. (De Boer et al 1963).

If we look at a recording of the eye movements of a rabbit on a torsion swing we notice the following:

a) The amplitude of the eye deviation is bigger at a smaller stimulus than when the stimulus amplitude is increased. Compare points A to D in fig. 16.
b) The number of nystagmus beats per period decreases as the stimulus decreases; compare points A and D in fig. 16.
c) The ratio between the total amplitude of the nystagmus and the amplitude of the eye deviation becomes smaller as the intensity of the stimulation decreases.

If we compare the results provoked by barbecue rotation, we find a partial similarity to the responses of the torsion-swing test. (fig. 14).

a) The amplitude of the eye deviation is bigger at a smaller stimulus and when the stimulus is increased, the amplitude decreases.
b) The number of nystagmus beats per period decreases with decreasing barbecue stimulus.
c) The ratio between the total amplitude of the nystagmus to the amplitude of the eye deviation becomes larger as the intensity of the stimulus decreases.

Let us try to explain these phenomena.

The provocation of the quick phase is the same in both cases, the torsion swing and the barbecue rotation. When the stimulus is small, the threshold for the quick phase is reached later than when the stimulus is large. This has

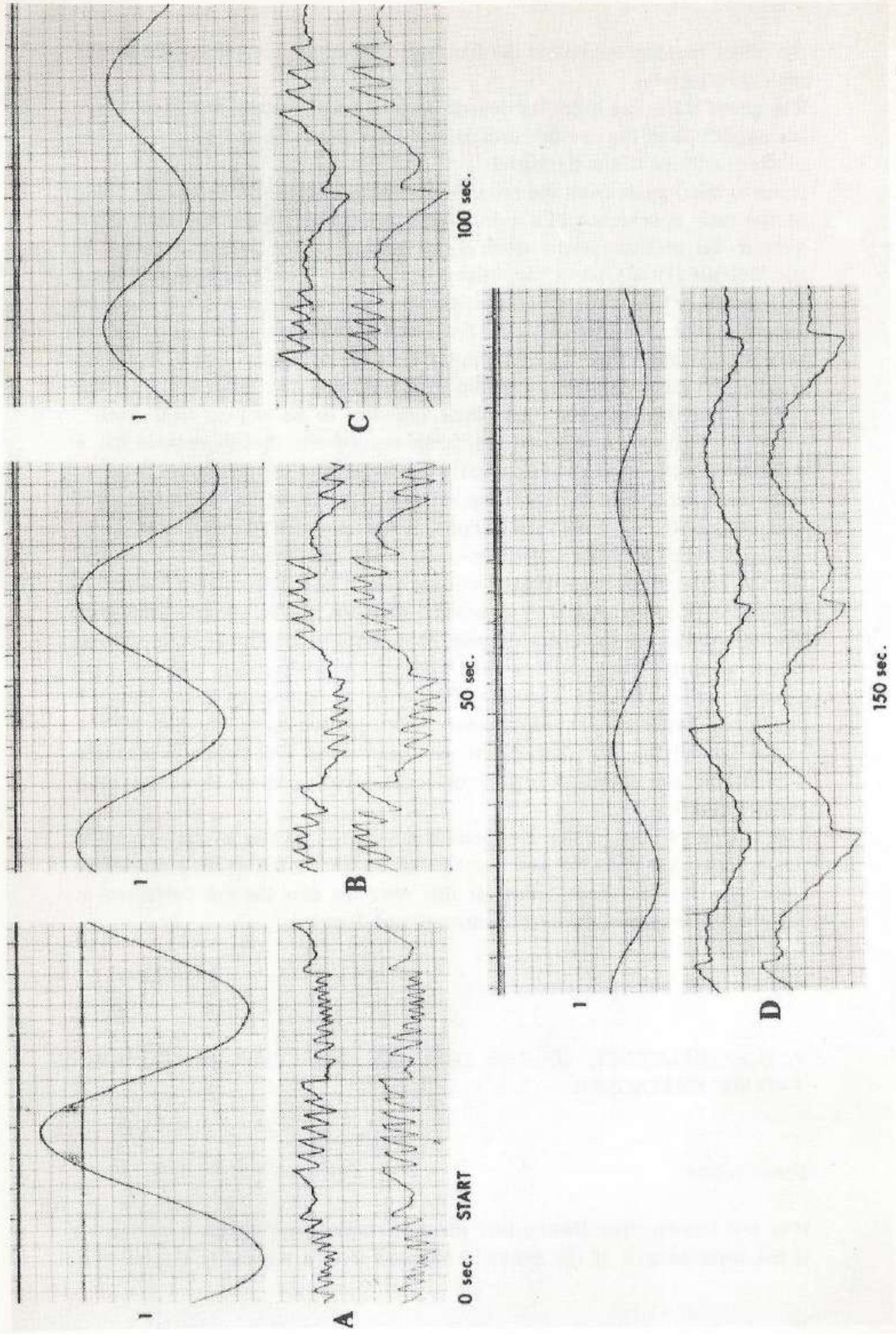

Fig. 16

Torsion swing recording of a rabbit.
1 = the intensity of the damped sinus.
A, B, C and D are the responses of the rabbit at various stages of the damped sinus. The amplitude of the compensatory eye movement is bigger when the stimulus is decreased.

the effect that the eye before the first beat is deviated more at smaller stimuli than at larger ones.

The above reasoning holds for speeds up to 4 sec./rotation. At higher speeds the amplitude of the eye deviation is reduced without a concomitant increase of the amplitude of the nystagmus.

It seems that, apart from the reduction of the amplitude of the eye deviation by the early appearance of a quick phase, there must be an inherent mechanism in the otolith system which is responsible for the latter decrease. Tait and McNally (1934) found "opposite compensatory" and (respectively) "anti-compensatory" eye movements resulting from a slow or quick tilt in the same direction about a horizontal axis. They suggest this could only mean that the utricular macula possesses two opposed modes of action. Schmidt (1963) relayed electrical impulses from the utricular nerves in frogs and is of the opinion that he recorded "feed back impulses to an ampula from itself". Flock (1964) described that the periphery of the otolith macula has a polarity opposite to the more centrally located area of the macula surface.

It appears that, when the barbecue rotation is increased beyond 4 sec./rotation, the otoliths stimulate these peripheral hair cells with an opposite polarity, causing a further decrease of the amplitude of the eye deviations. We shall later discuss (under the chapter dealing with the effects of fentanyl on the barbecue responses) that this view is in agreement with our results, i.e. that there is an inherent ability of the otolith organs to reduce the amplitude of eye movements when the stimulus increases. The effects observed are not due to a pendular action, because a phase shift is not noticed. (similar to the damped-pendulum theory of the semicircular canals, see van Egmond, et al (1943).

In the light of the above arguments we can conclude that the reduced amplitude of the eye deviation is probably caused by a central as well as by a peripheral action.

That the amplitude of the eye deviation becomes smaller at faster angular speeds does not indicate that mechanical forces on the eyeball materially contribute to the eye deviation. If this were the case the eye deviations at higher angular speeds, should increase and not decrease.

7. THE INFLUENCE OF THE GRAVITY DIRECTION ON POST-ROTATORY NYSTAGMUS

Introduction

It is well known since Bárány that the post-rotatory nystagmus is modulated if the rotation axis of the animal is changed from a vertical to a horizontal plane. However, it is not clear whether the direction of gravity influences the post-rotatory nystagmus when the rotation axis is kept in a horizontal plane. Guedry (1964), Correia and Guedry (1964), Benson (1962, 1967) and Benson and Bodin 1965, 1966 reported no difference in post-rotatory responses when test subjects were stopped in different positions in relation to the direction of "g", i.e. supine, prone or in one of the side positions. We performed a series of experiments in which the axis of rotation remained horizontal, and where the animals were stopped in different positions so as to change the direction of gravity in relation to the labyrinths.

Execution

Rabbits were rotated about their longitudinal horizontal axis at different angular speeds. The rotation velocities varied in steps from 36°-72°-144°/sec. After the nystagmus provoked by the acceleration ceased, the turntable was switched off in various stop positions, e.g. prone, supine and in both lateral positions. The different stop positions could be achieved within a ±10° accuracy. The impulse initiated a post-rotatory nystagmus. We measured both the duration of the nystagmus and the maximal speed of the slow phase of the nystagmus as a function of the speed.

The order in which we used the various stop positions varied to a randomized design. The experiment ranged over 20 normal animals.

Observation

We shall discuss the salient features of each of the different stop positions separately. First, we discuss results obtained in a prone stop-position. In hardly any case did we notice a post-rotatory nystagmus (fig. 17). In three cases, though, we counted a few beats, following a rotation speed of 144°/sec. The duration of the nystagmus was ca. 2 sec. after the stop. Slower velocities did not provoke post-rotatory responses.

When the animals were stopped in a supine position we noticed in all except two a post-rotatory response (fig. 17). We saw no difference whether the rotation had been clockwise or counter-clockwise. The direction of the nystagmus was inverted compared to that in the prone position. The nystagmus was equal for both eyes. The number of beats had a clear relationship to the size of the stimulus. When the rotation speed was 36°/sec., 6 beats were counted over 8 seconds. When the rotation speed was increased to 72°/sec. the mean amount was 8 beats over 10 sec. and when the barbecue rotation was speeded up to 144°/sec. the number of beats doubled to 15; this nystagmus lasted even 14 seconds.

Next we describe observations in both lateral positions. See fig. 18; the animal

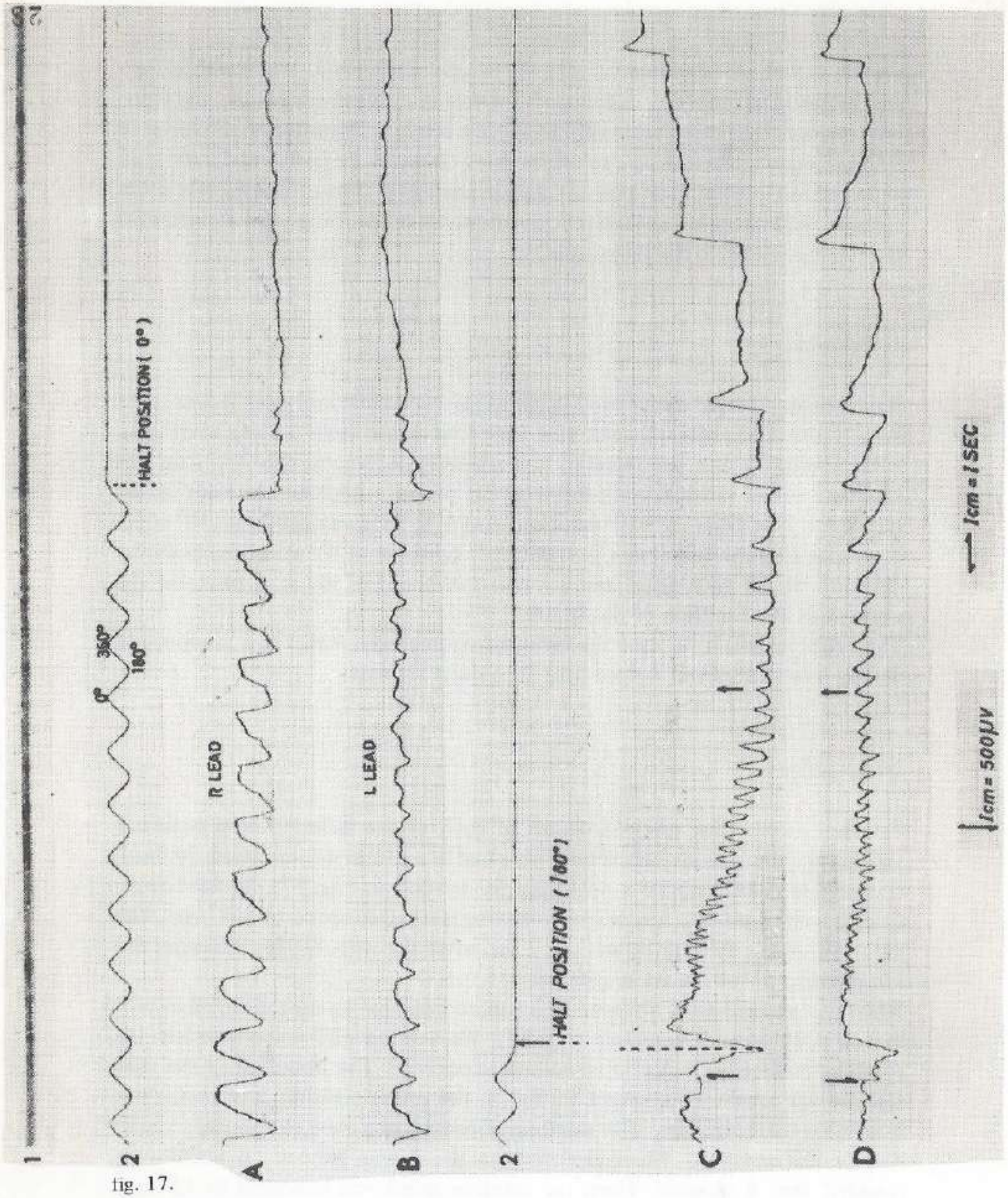

fig. 17.

The influence of the change of the direction of gravity on the post-rotatory nystagmus
1 = time in seconds.
2 = barbecue rotation.
A and B = post-rotatory responses when the rabbit is stopped in a prone position.
C and D = post-rotatory responses when the rabbit is stopped in a supine position.
The nystagmus in the supine position is much intenser than in the prone position.

was stopped while either the left or right side was facing downward. In general, we noticed a smaller response in the lateral positions than in the supine position. Ten of the 20 tested animals had a measurable response. The upper eye always responded with a smaller intensity than the lower one as regards duration and maximal speed of the slow phase. Clockwise and counter-clockwise rotations gave the same results. The nystagmus for the lower eye after a stop at 144°/sec., had a mean value of ten beats, a maximal speed of the slow phase of 50°/sec. and lasted for 7 seconds.

The upper eye responded less intensely. The mean amount of beats was five over a duration of 4 sec., and the beats had a maximal speed of the slow phase of 10°/sec.

In conclusion we can state the following:

a) Practically no post-rotatory nystagmus occurred if an animal was stopped in a prone position.
b) An intense nystagmus appeared if the same animals were stopped in a supine position.
c) A distinct difference between the upper and lower eye appeared as regards frequency of beats and maximal speed of the slow phase when the animal was stopped in a lateral position.

Discussion

The post-rotatory responses about a horizontal axis are rather strange if compared to similar effects when the axis of rotation is vertical as in cupulometry, the torsion swing, or Bárány's test. One must bear in mind that during rotation about vertical axis the gravity effects are constant both during and after rotation. The behaviour of the post-rotatory responses about a horizontal axis cannot be explained by cupular responses alone. For if the cupula were gravity sensitive, gravity should have aided cupular activity in one or the other position, and this would become noticeable in the nystagmus as a difference between a clockwise and a counter-clockwise rotation. This is contrary to experimental evidence, hence the assumption is not tenable.

Neither is it possible to maintain that the effects are exclusively due to otolithic effects, in view of the dependence on rotationspeed (Bergstedt 1967 Ciba Symposium). During the stop impulse after barbecue rotation the canals and otoliths simultaneously signal a change in angular velocity and in position. These two informations might contradict each other in different stop positions. The influence of the direction of gravity on the post-rotatory nystagmus is like a modulation. Its mechanism may be peripheral (otolithic or cupular), kinestetic (Guedry 1964) or an effect of central regulation (Groen 1967).

Our experiments do not favour the view that gravity has any direct effect on cupular responses for this does not explain the differences in responses of the

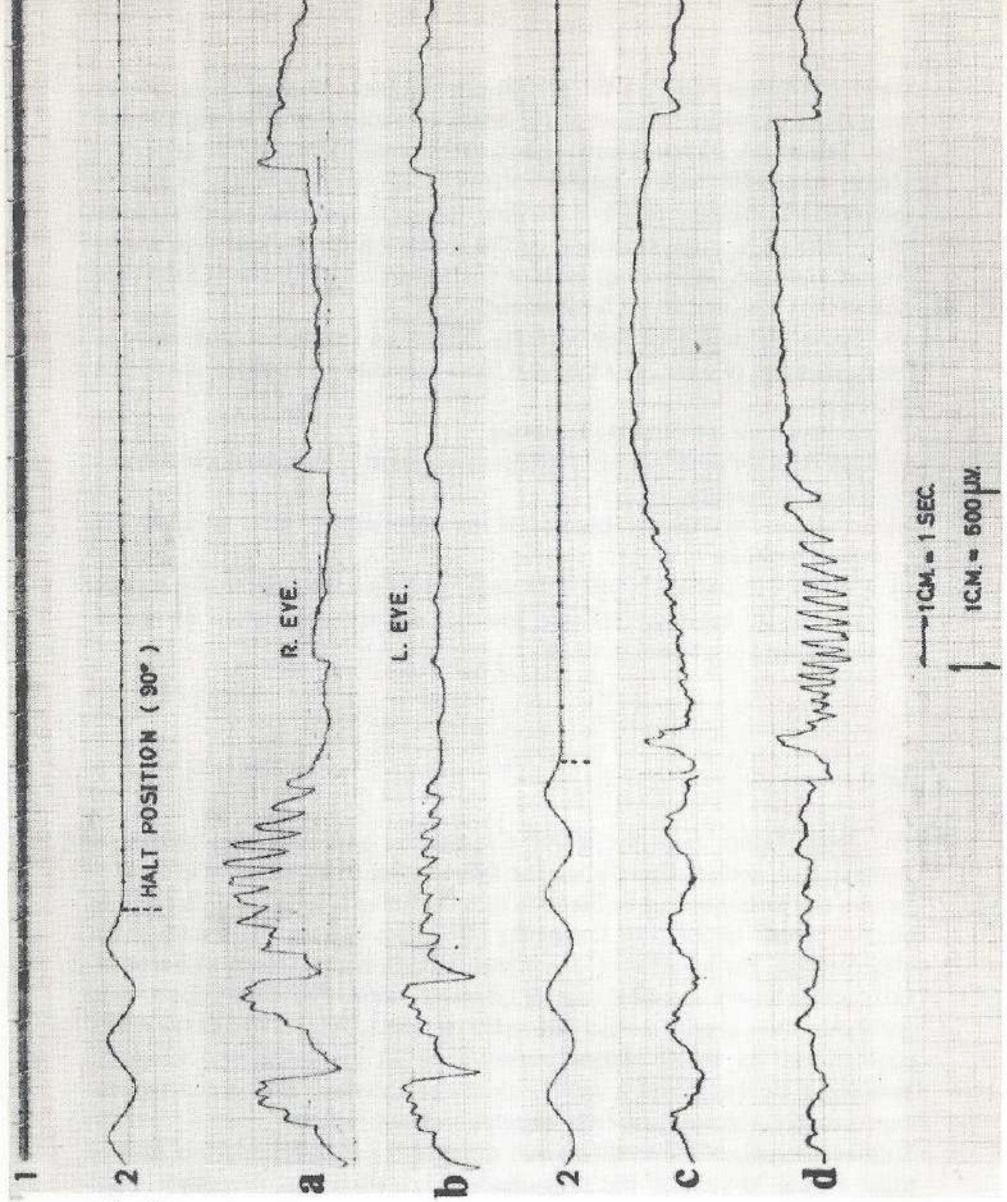

Fig. 18

The influence of the change of the direction of gravity on post-rotatory nystagmus.
1 = time in seconds.
2 = barbecue rotation.
A and B = post-rotatory nystagmus when the rabbit is stopped in the right side position; the right eye facing downwards.
C and D = post-rotatory nystagmus when the rabbit is stopped in the left side position; the left eye (D) facing downwards.
In both side positions the lower eye had an intenser nystagmus, regarding the amount of beats and the maximal slow phase value.

upper and lower eye when the rabbit is stopped in a lateral position. We are of the opinion that the otolith system is responsible for these modulating effects on cupular responses.

The mechanism will probably be neural and its location remains a matter of conjecture.

8a). THE EFFECTS OF FENTANYL ON LABYRINTH REFLEXES PROVOKED BY BARBECUE ROTATION

The nystagmus provoked by both a torsion swing and a barbecue rotation, originate from local exitatory processes in the labyrinth. It is therefore justified to compare the results of both stimulation patterns in order to determine the effects of drugs upon labyrinth reflexes. The reaction to the torsion swing are well studied in normal as well as in drugged subjects, so that these can be regarded as models for purposes of comparison.

The drug fentanyl is known as a morphine-like substance and used as an adjuvant to local or general anaesthesia. (Janssen 1963 and Erba 1965 describe it as an analgesic belonging to the group of neuroleptica).

When the drug is given intramuscularly (i.m.) to experimental animals the effects can be noticed after about 20 min. They are lassitude and placidness. Although it renders the animals co-operative for handling, they still seem to be fully aware of any painful interventions. It does not induce a central or positional nystagmus. The antidote is nalorphine according to the accompanying literature.

Method

For this experiment we used 20 normal rabbits which were fastened to the rotation table in the usual way. After the rabbits have undergone several initial examinations on the torsion swing and by barbecue rotation, 150 mg. fentanyl was administered i.m. At various intervals following the injection the animals were again tested to torsion-swing movement and barbecue rotation.

Results

The beginning of the effect of the drug was well noticed after 15 min. A maximal effect was observed after 30 min. The effect lasted for more than four hours. The results obtained indicate that this drug increased the threshold of the quick phase of the nystagmus in the torsion-swing test. The peripheral-labyrinth activity seemed unimpeded since the slow eye movements were still present on the recording (fig. 19). When the barbecue responses are reviewed, the same general effect was noticed, namely that the quick phase of the nystagmus was abolished so as to let the nystagmus beats disappear. The amplitude of the slow eye deviation had increased as is to be expected when the quick phase is absent.

Earlier in this work we mentioned that approximately 10% of the animals react to the barbecue stimulus with only an eye deviation without concomitant nystagmus beats. In these animals one would not expect an increase of the amplitude if fentanyl is administered, because there originally was no quick phase to "reduce" the amplitude of the eye deviation. This was found to be true indeed. After injection of these animals we noticed no increase of the amplitude of the eye deviation.

When the rotation speed was increased, the amplitude of the eye deviation decreased in accordance with the tendencies mentioned earlier. We also noticed that the difference of amplitude between the left and right eye remained and that the left eye responded to a clockwise rotation with a bigger amplitude than the right one and vice versa. These observations would suggest that the mechanism which is responsible for this difference in the eye deviations is of peripheral origin, if we assume that the quick phase of nystagmus - the one that is abolished by the drug - is of central origin. (Alexander's Law 1929, Jongkees and Philipszoon 1962, 1964, Philipszoon 1962, Bos et al 1963).

The discovery that the eyes only respond with a increased amplitude of the slow eye deviation without nystagmus beats when this drug is administered, makes it necessary now to discuss some matters concerning the basis of our methodology. In how far do mechanical forces influence the movements of the eyeball in its orbit? This matter is of importance during barbecue-rotation experiments where the quick beats are abolished.

Kompanejetz (1925) studied the problem in how far direct mechanical factors can contribute to the eye deviation when the head is inclined or declined from the vertical. For this purpose he used unilaterally ophthalmoplegic patients

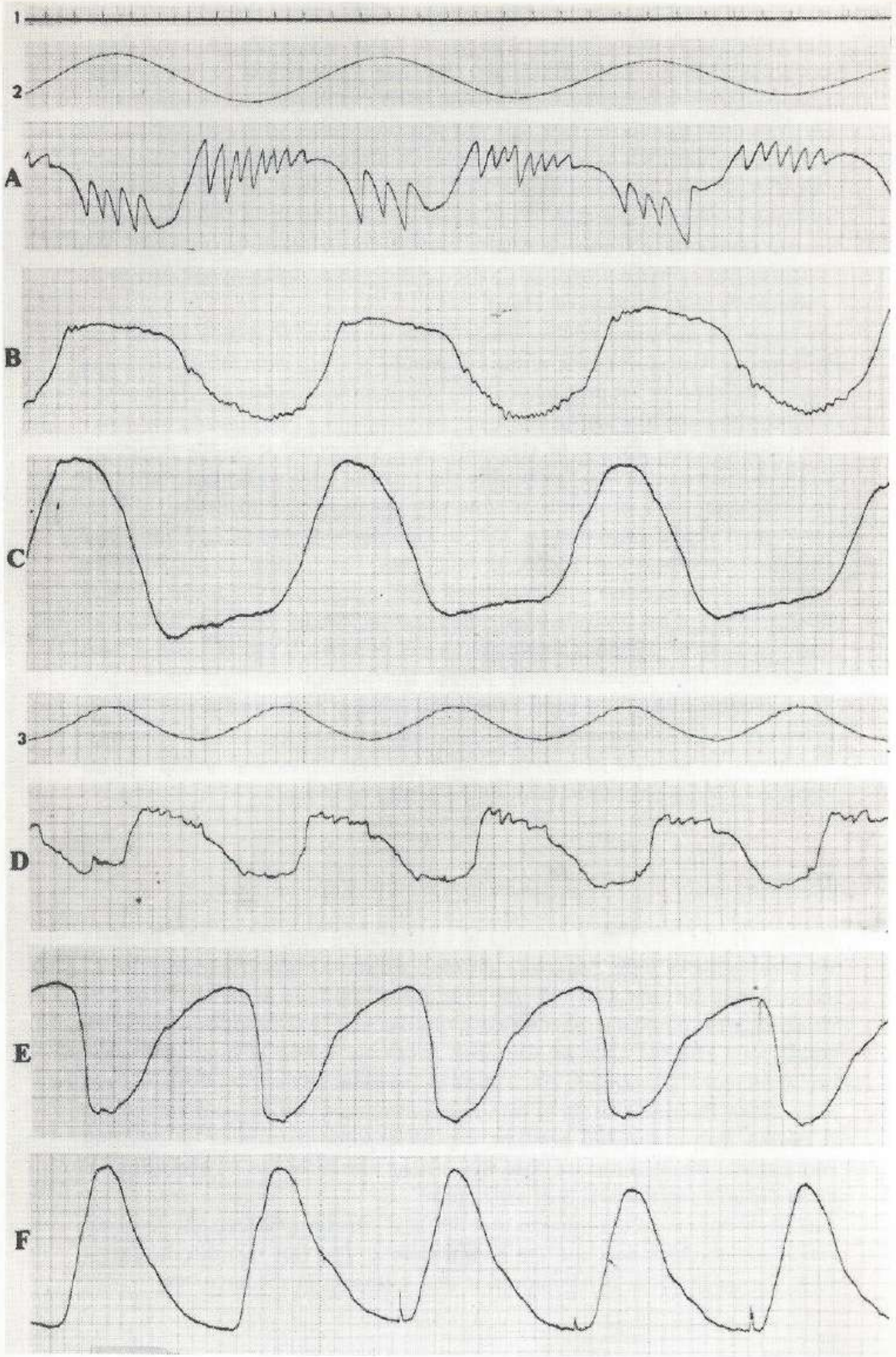

Fig. 19.

The effects of fentanyl on labyrinth responses:

1. Time in seconds.
2. Torsion-swing stimulus.
3. Barbecue-rotation stimulus.

A. Torsion-swing response of an undrugged rabbit.
B. Torsion-swing recording 20 min. after the injection of fentanyl.
C. Torsion-swing recording 30 min. after the injection of fentanyl.
D. Barbecue response in an undrugged animal.
E. Barbecue response 20 min. after the fentanyl injection.
F. Barbecue response 30 min. after the fentanyl injection.

and subjected them to different angles of lateral tilting. He observed that a deviation from the vertical less than 10° had no influence on the counter-rolling of the paralysed eye and between 10-60° tilting the eye deviated 4-9°. He attributed this to the fact that the centre of gravity of the eyeball lies off the rotation axis. We have some remarks on his conclusions. First his experiments ranges over patients with a total ophthalmoplegia. In normal subjects eye-muscle tonus could counteract the effect found to a great extent. Second in our experiments we worked with rabbits which have a lateral sight. The centre of gravity has not necessarily the same position and does not essentially provoke the same mechanical effect.

To study the influence of the change of the direction of gravity on the eyeballs per se, the movements of the eye should be freed from labyrinthine and central influences. For this purpose we relied on a complete paralysis of the animal with flaxedil 2 mg/kg i.v.

We canulized the trachea of the rabbit and connected it to the respirator. After this the animal was fastened to the rotation table whilst horizontal and vertical leads were attached. In this way we were able to notice whether mechanical forces provoked by the rotation about a vertical and horizontal axis could influence movements of the eyeball. Consecutively a torsion-swing test and a barbecue test were performed. The recording of the former showed no movement of the eyeballs, whilst the latter indicated minimal movement of both eyeballs of 2-3 mm. amplitude (1 cm. = 500 μ V fig. 20). When both movements were simultaneously tested, the pattern remained unchanged. These findings make it doubtful whether the change in the direction of gravity in relation to the labyrinths could mechanically have influenced our recordings. The more so because in normal animals eye-muscle tension would oppose rotation of the eyeball in its orbit under gravity influence.

Discussion

Dowdy, et al (1965) used fentanyl in combination with droperidol in acute Ménière's attacks with "dramatic results" within 10 min. following the injection. They did not specify the site of action of the drug. In our investigation we attempted to find out whether the cupulo-ocular and otolith-ocular reflex arches were effected alike by this drug. From our results it appears that the otolith-ocular reflex arch is acted upon in the same way as the cupular-ocular arch. These findings also fit in with Alexander's Law, which states: if the eye is moved into a deviated position, e.g. in response to cupular or otolithic stimulation, the chances are that the central threshold for a quick phase is exceeded and a nystagmus beat will appear.

Janssen (1963) is of the opinion that fentanyl selectively affects the formatio reticularis, the thalamus and the hypothalamus. The fact that this drug abolishes the quick phase of nystagmus is one argument in favour of the notion

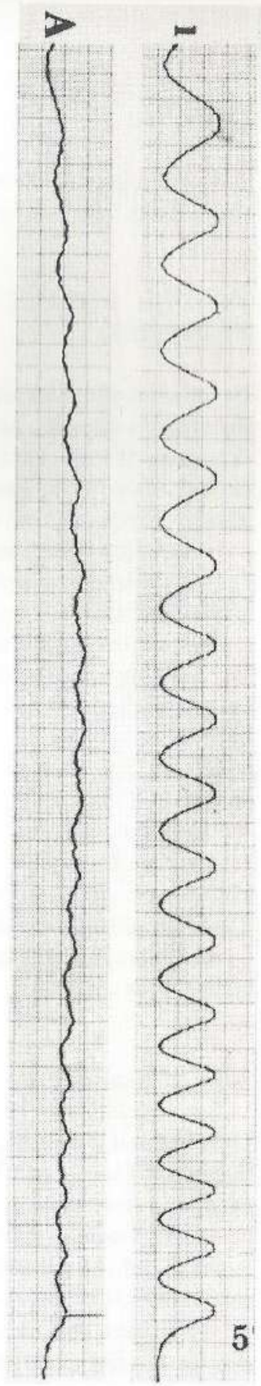

Fig. 20.

The effects of flaxedil on barbecue responses:

1. Barbecue rotation.
A. Barbecue responses after the injection of flaxedil.

that the quick phase is of central origin and not due to a simple proprioceptive reflex arch.

Conclusions

Our findings suggest that the effect of fentanyl is restricted to the quick phase and appears to have a central inhibitory effect.

8b). THE EFFECTS OF SODIUM BICARBONATE ON LABYRINTH RESPONSES

In order to eliminate otolith function we also tried to dissolve the otoliths by intravenous injection of a solution of $Na(HCO_2)_2$.

Hasegawa (1949, 1955 and 1963) is of the opinion that his solution can abolish some of the otolith functions, such as the perception of linear accelerations. The perception of gravity is said to be still present. ("Keinen Reflex auf Linearbewegung, hingegen normalen Reflex auf Lageveränderung"). He explains this phenomena on the basis that the otoliths are completely dissolved and that the ground substance between the otoliths and the sensory epithelium is changed when the labyrinth is viewed electron-microscopically. We used five animals, all of which received 10 cc. of an 8% solution for five successive days intravenously. Each animal was tested twice per hour for three hours after the injection on each of the five following days. The above author's results are still open for conjecture since except for the habituation response decline (r.d.) we could not detect the disappearance of the otolith function. We used the barbecue stimulus as well as the parallel-swing test. Our results coincide with the findings of, among others, Giaccai and Carle (1951) and Philipszoon and v.d. Laarse (1962).

There is ample proof that sodium bicarbonate does not effect otolith responses to linear acceleration and does not interfere with the reflexes provoked by barbecue rotation.

8c). CINNARIZINE

The effects of this drug are so well studied by Philipszoon (1959), Bos (1962), Oosterveld (1963) and Philipszoon and Jongkees (1964), that we hardly need to extend their experiments, except for the effect of this drug on barbecue-rotation nystagmus. After administration of this drug the eye movements were reduced and the per-rotatory nystagmus even disappeared. Post-rotatory responses in all four positions were partly suppressed. The changes brought about by cinnarizine and fentanyl to the barbecue responses demonstrate a difference in the site of action. Both suppress the appearance of nystagmus but the mechanism of both drugs differ, cinnarizine acting both centrally and peripherally whilst fentanyl acts centrally and is restricted to the fast phase.

8d). THE EFFECTS OF ALCOHOL ON THE LABYRINTH REFLEXES PROVOKED BY THE BARBECUE ROTATION

In the light of current facts, our knowledge of positional alcohol nystagmus (p.a.n.) is far from complete. During barbecue rotation the labyrinth changes position through 360° in relation to gravity. It offers an additional method to study the effects of alcohol on labyrinth responses under different gravity directions. If the canals are rendered gravity-sensitive by alcohol, as has been stated by Money (1962, 1965) and Nito (1964), we may expect that the canals system can signal an alteration of the gravity direction which may eventually lead to a change in the nystagmus provoked by the alcohol.

Execution

For this investigation we used ten normal rabbits. They were given a torsion-swing test and a barbecue-rotation test before they were intoxicated. These vestibular tests were given in order to compare pre- and post-intoxication reactions.

2.5 cc/kg ethanol 96% was administered intravenously (i.v.) in a 20% diluted solution with normal saline. After this injection the vein was flushed with normal saline to prevent thrombophlebitis. In most cases p.a.n. was noticed to appear within 10 minutes after the administration of alcohol. The animals were observed in all four positions for p.a.n. namely supine, prone and both side positions.

Observations

When the rabbit was positioned either in supine or in a lateral position, p.a.n. appeared. The nystagmus direction changed in accordance with the position occupied by the rabbit. In both lateral positions the direction of the nystagmus was opposite to each other. Aschan, et al (1964) reported that in patients exhibiting p.a.n. the direction of the fast phase was to the left if the patient was lying on his left side or to the right if he was lying on his right side. In our experiments no response was noticed in the prone position. We used constant rotation about a vertical axis as well as barbecue rotation, in order to study the effects on p.a.n. In the first few barbecue rotations we saw p.a.n. superimposed upon the normal response. But after a few rotations p.a.n. was suppressed and it vanished after the fourth rotation. (See fig. 21.) During constant barbecue rotation no p.a.n. was observed any more.

Apart from the barbecue nystagmus, a few additional beats were observed (fig. 21). These recordings were also checked with faster paper speeds as described earlier under the heading: "Identification of Nystagmus". In some cases we noticed that the p.a.n. in certain positions could only be provoked after an initial movement. This is well demonstrated in the lower part of fig. 21. The animal occupied a supine position. No nystagmus was initially present. As soon as the barbecue rotation commenced, the p.a.n. appeared. After a few rotations it was suppressed again by otolith activity. Not only was the movement necessary to provoke the nystagmus, it also caused its direction to invert even when the direction of gravity was not inverted at all. (See the arrow heads in the figure.) This change of direction of nystagmus seems to depend on the initial movement. Koella (1948, 1949), Bos (1962) and Jongkees and Philipszoon (1964) found that otoliths can induce a change of direction of an already present nystagmus. The latter three authors performed unilateral labyrinthectomies on rabbits and observed a nystagmus of which the direction depends on the static position. This view is also in accordance with our conclusion that a peripheral nystagmus can be changed in direction by the otoliths. We will come back to this point under the heading "Unilateral labyrinthectomy".

Our experiments thus indicate that the position as well as the movement to obtain the position is important for p.a.n. As one notices there exists a clear inhibitory effect of otolith stimulation on p.a.n. In how far is this inhibitory effect responsible for the absence of p.a.n. in prone position? In other words, is p.a.n. continuously present and only suppressed in certain positions by the inhibitory effect of the otoliths? We are of the opinion that p.a.n. can indeed occur in all positions. In fig. 21 one notices that if the animal reaches the prone position during a barbecue rotation, p.a.n. is present but is inhibited again after a few rotations. It must be noted that at the instant of prone position with position nystagmus a (slow) eye deviation - typical for the barbecue rotation - was present as well.

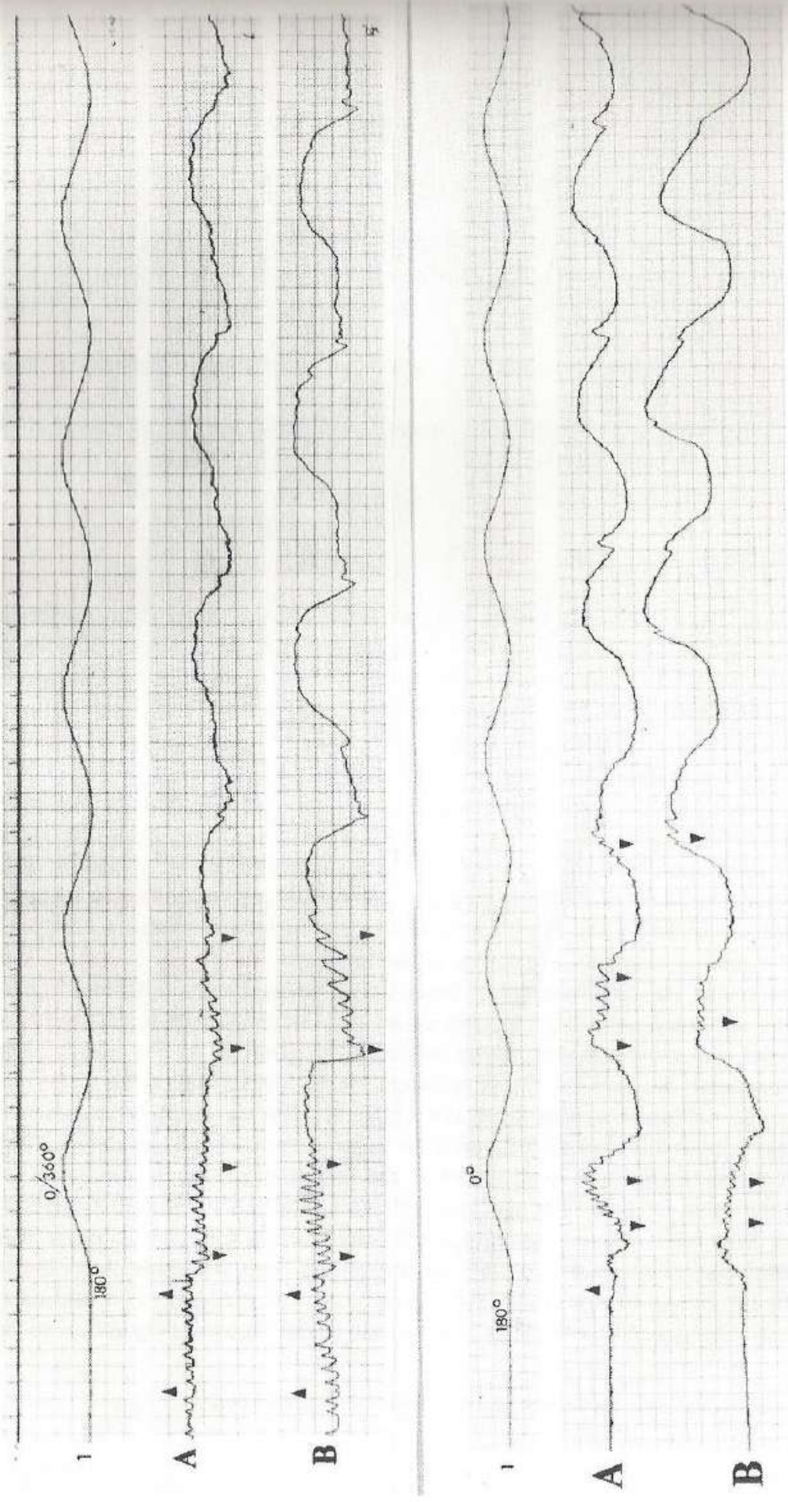

Fig. 21.

The effect of the barbecue rotation on p.a.n. 1 = barbecue rotation, A = right eye recording, B = left eye recording.
The upper figure demonstrates the following: 1. The direction of p.a.n. inverted by the start movement of the rotation and not by the inversion of the "g" direction. 2. The p.a.n. remains unidirectional when the "g" direction inverts during the first few rotations 3. After a few rotations p.a.n. is almost completely suppressed. The lower figure demonstrates an absence of p.a.n. in the supine position. As soon as the barbecue rotation commenced the p.a.n. reappeared.

In conclusion we may say:

a. P.a.n. 1* is principally related to the orientation of the animal, namely in the prone position no nystagmus occurred, while an intense response occurred in both lateral and supine positions.

b. During the first few barbecue rotations p.a.n. was noticed in all positions (including the prone position).

c. No change of direction of the nystagmus occurred during the first few rotations even though different positions were occupied during rotation. A change in direction of the nystagmus was only obtained in the initial movement.

d. During the later per-rotational phase p.a.n. was nearly completely suppressed.

e. The normal type of barbecue response appeared under alcohol intoxication as somewhat reduced.

Discussion

Let us return to the hypothesis that the cupula (or, for that matter, the whole canal system) would be rendered "g" sensitive under the influence of alcohol. If this were so the direction of the nystagmus would rhythmically change in accordance with the change of the direction of gravity. Since this has not been found in our experiments the hypothesis should be rejected.

The fact that p.a.n. is suppressed only during rotation and not, when supine or lateral positions are continuously occupied, suggests that reorientation (re-positioning) has a stronger suppressive effect than position per se. While the barbecue rotation is lasting p.a.n. is suppressed in all positions. This stresses the point that the influence of alcohol should be assessed in a kinetic situation in which the otolith system is activated by a continuous change of the direction of gravity in relation to the labyrinth.

Concerning the methodology of Money et al, we have some criticisms to add. They abolished p.a.n. by blocking all six semicircular canals in cats and concluded that the canal system was rendered "g" sensitive by the alcohol. The canals were blocked by "bone splinters" made with a high-speed drill. This may be sufficient to inactivate the canals but the utricle may be rendered inactive as well (either by leakage or by accumulation of bone splinters). Then the sacculus may have been spared at the same time. This is possible because of the valve of Bast. The so called remaining "utricular" function might in fact have been saccular function. Furthermore, their test used to prove that otolith function was still intact is inappropriate. Their test made use of the so called "Sprung Bereitschaft". After having cut the utricular nerve and dammaged the saccule, Versteegh (1927) still found this jumping reflex to be

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*P.a.n. 1 is the p.a.n. during the first few hours after intoxication.

present. We do not suggest that p.a.n. comes from the peripheral labyrinth since the exact mechanism of alcohol is not yet established, but we do want to stress the point that the otoliths can modulate and even suppress p.a.n. We cannot substantiate the fact that the canals are rendered gravity-sensitive by alcohol. A more plausible hypothesis, for the moment at least, would be that the otoliths modulate a centrally provoked nystagmus both in amplitude and direction, depending on the position in space. We are of the opinion that during intoxication with alcohol a nystagmus tendency is continuously present and it is only released in certain positions. Our views agree with those of Aschan, et al (1964) that the site of p.a.n. must be sought more centrally. This might explain why cinnarizine did not have any effect on p.a.n. in the experiments performed by Bos and Philipszoon (1963) and Jongkees and Philipszoon (1964).

9a). SURGICAL INTERVENTIONS; APPROACH TO A PARTIAL OR TOTAL LABYRINTHECTOMY

Introduction

In order to study the function of the saccule, the utricle and the semicircular canals it is valuable to eliminate selectively the functions of the various suborgans.

Procedure

In this serie we used rabbits from 6 - 12 months old and weighing about 2 kg.; we avoided very young ones because of their restlessness. Pre-operative torsion-swing, parallel-swing and barbecue responses were recorded, in order to compare them with post-operative responses. We used the approach to the labyrinth as described by De Kleijn and Versteegh (1929, 1927) which served for all our surgical interventions on the labyrinth. The animals were fixed in supine position on the rotation table, which was used as an operation table. This was done so that we can check qualitatively the labyrinth responses at any stage of the operation, by rotation about a vertical as well as a horizontal axis. For general anaesthesia we used sodium-nembutal, $^1/_2$ ml/kg., this dosis gives a very light anaesthesia. To improve our view we used a Zeiss zoom microscope (type 2), of which the maximum magnification is forty times.

The operation can be divided into three stages:

a. approach to the bulla, fig. 22;

b. opening of the middle ear, fig. 23 and
c. proceeding to the inner ear, fig. 24.

a. After about a $1\frac{1}{2}$ cm. incision has been made medial to the angle of the jaw, we freed the bulla by blunt dissection of the overlying soft tissue.
b. We opened the bulla with a drill and a bone nibbler so that we finally had a good view of the middle ear, especially the promontory where the stapes crura indicates the site of the oval window.
c. We removed the promontory either by inserting a small hooklet into the oval window to tear it open or by using a small drill. Lesions to the stapedeal artery sometimes lead to troublesome but fortunately short-lasting bleedings. After removal of the bony fragments, the utricle and its nerve are clearly visible, lying on the membrana limitans. The otolith hanging

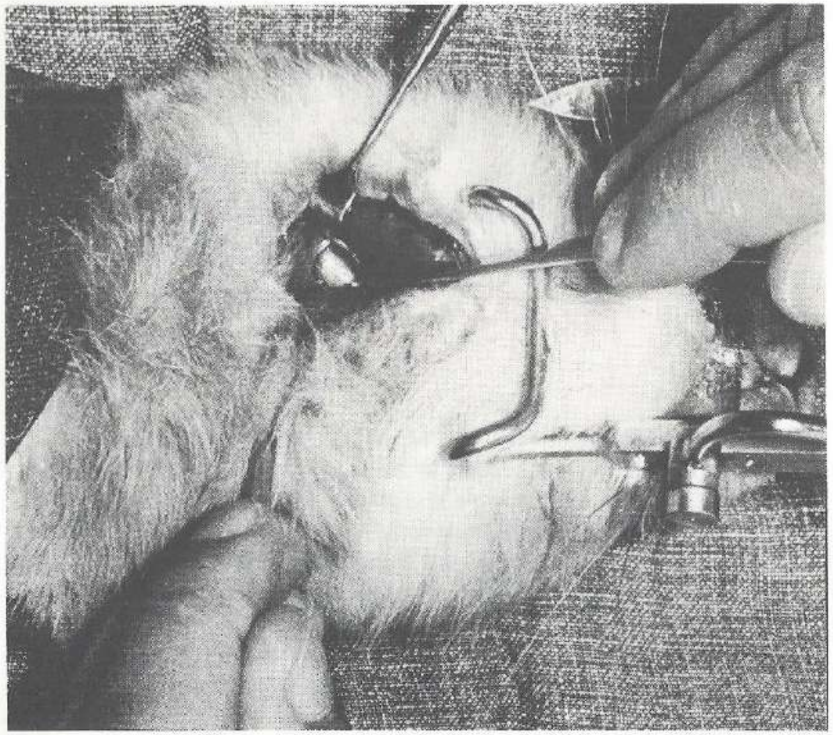


Fig. 22.

Stage one of the operation; freeing the bulla. The rabbit occupies a supine position. The bulla is seen in the depth.

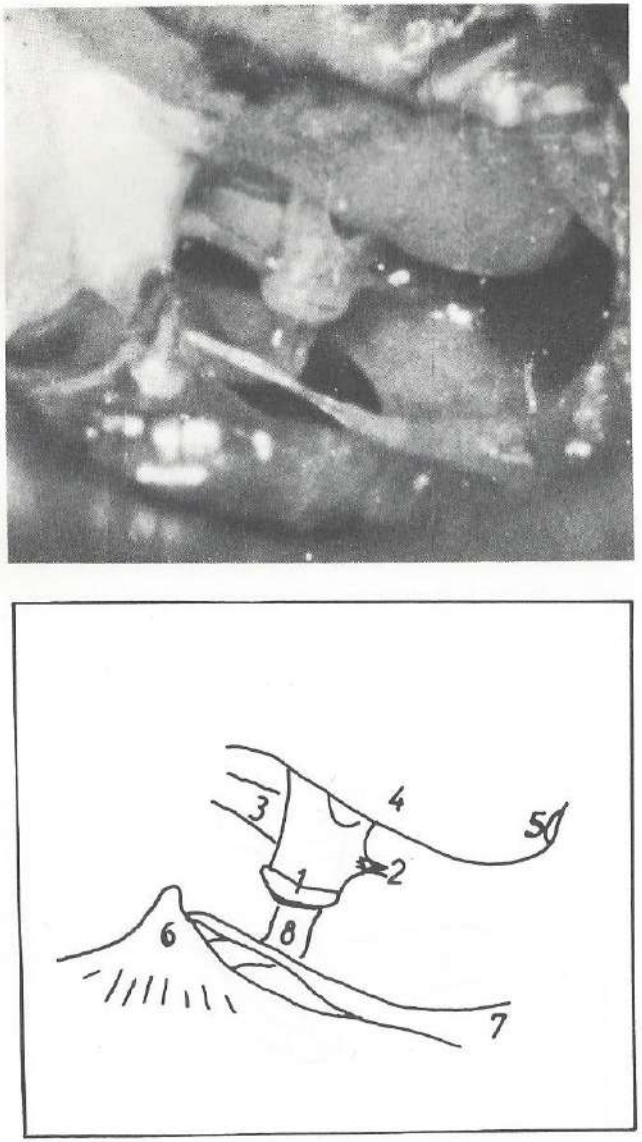


Fig. 23.

Stage two; opening of the middle ear.
The stapes indicates the site of the oval window.
1 = stapes-incus joint.
2 = musculus stapedius.
3 = facial nerve.
4 = promontory.
5 = round window.
6 = eardrum.
7 = musculus tensor tympani.
8 = incus.

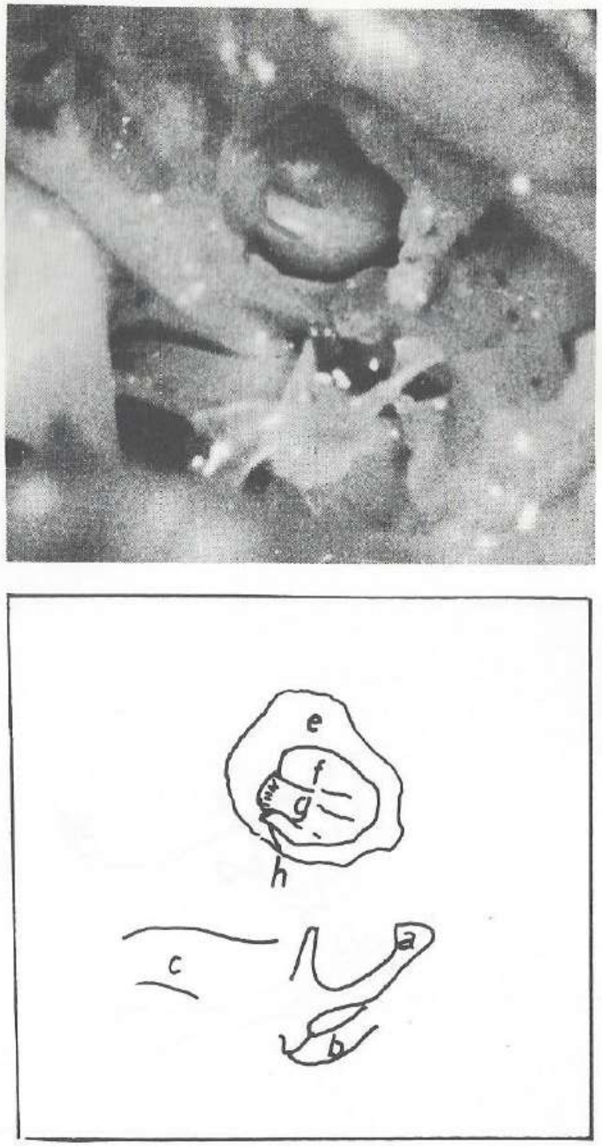


Fig. 24.

Operational view of the inner-ear:
a = Crura of stapes.
b = Incus, lenticular process.
c = Facial nerve.
e = Limiting membrane.
f = Utricular macula.
g = Utricular nerve.
h = Nerve from the lateral semicircular canal.

When the utricular nerve is cut the nerve from the lateral semicircular canal can easily be damaged and this can lead to a failure of the operation.

from the utricular macula is not visible from this angle. The membrane of the saccule, which is slightly ventral of the utricle (fig. 25), is seen if the entrance to the inner ear is adequate. The saccular macula is approximately in a vertical plane and by moving the hooklet a few times back and forth, we could destroy the saccule and its macula. By the loss of endolymph the saccule and the cochlea are destroyed while the canals and the utricle are still in a normal functional condition. This is due to the valve of Bast, a fold in the utricular floor, which passively seals the canals and utricle

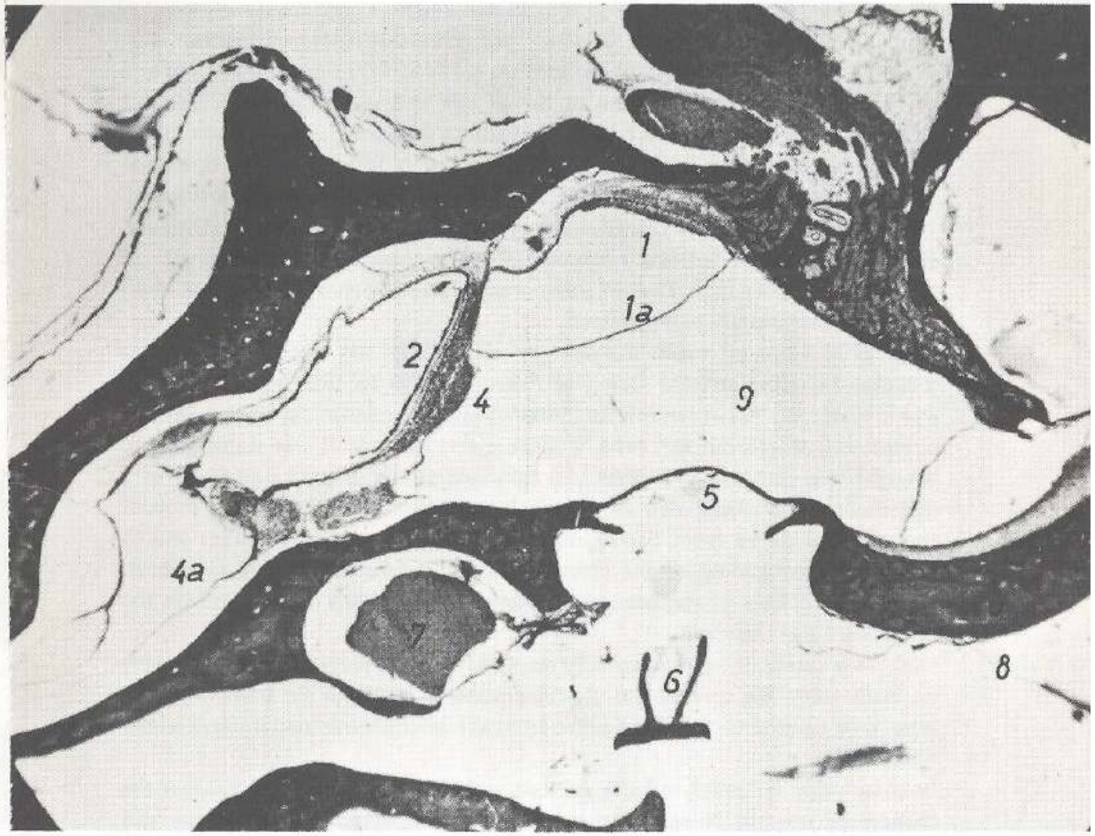


Fig. 25.

Section through the inner-ear structures.
1 = Saccular macula; 1a = Saccular membrane.
2 = Utricular macula; 3 = Cupula of the lateral semicircular canal.
4 = Utricular nerve; 4a = Lateral semicircular canal.
5 = Oval window; 6 = Remnants of the stapes crurae.
7 = Facial nerve; 8 = Promontory; 9 = Cochlea.

from the cochlea and saccule if the pressure is lowered in the latter (James, 1968). The functional integrity of the canals and utricle could qualitatively be tested at this stage of the operation by comparing responses to torsion-swing and barbecue rotations during operation to the pre-operative nystagmograms. From here we proceeded either to:

a. mechanical destruction of the entire labyrinth;
b. stimulation of the utricle and its nerve or
c. severing of the utricular nerve, thus creating a partial labyrinthectomy with only the canals functionally intact.

ad a. To ensure a complete labyrinthectomy in case a we poured a few drops of 70% alcohol into the inner ear after mechanical destruction was completed. A direct proof of a successful extirpation is found in the sudden tonic spasm of all four extremities as soon as the utricle and membraneous canals are destroyed and second in a typical nystagmus appearing in both eyes. If the animal has recovered from the anaesthesia and is freed from the operation table it violently turns about its longitudinal axis. When the rabbit is suspended in the air the head is turned sideways with the removed side underneath. Recordings were performed 4-6 hours after the anaesthesia had worn off and repeated the next day. Two to three weeks later the spontaneous vestibular symptoms are usually compensated.

ad b. In a series of seven animals we electrically stimulated the utricular macula, the nerve and the stump of the nerve after an extirpation. To avoid eye tremors the facial nerve was transsected in its middle ear course. As the stimulating electrode we used a steel electrode which was stabilized and brought into position by means of a micro-manipulator under guidance of a microscope. The stimulated area was covered with liquid paraffin, to prevent the utricular nerve from drying, to isolate the electrode still further and to prevent the spreading of the electrical stimulus (Andersson and Gernandt, 1950). The effects of mechanical pressure on the otolith macula and on the nerve were also observed.

ad c. In a series of more than fifty animals we sectioned the utricular nerve on both sides. We severed the utricular nerve as it enters the bony wall. We were very careful to spare the nerve from the lateral semicircular canal which runs nearby.

In some cases we paralysed the animals with 1 mg/kg flaxedil to increase the chances of success. Needless to say that we performed a tracheotomy and connected the animal to a respirator in these cases. The wound was flushed with penicillin solution and closed with silk sutures. The eardrums were left intact to avoid infection.

After the animal had sufficiently recovered from the anaesthesia we checked the success of the operation by performing a torsion-swing test to test the integrity of the lateral semicircular canals, a parallel-swing test to see whether there was otolith function and lastly we subjected the animals to a barbecue rotation. Only intact canal function together with a negative response obtained on the parallel swing and an absence of positional nystagmus led us to judge the operation as a success.

After the desired recordings were performed, the animals were killed in order to perform a post-mortem investigation of our operation. The wound was opened and the inner ear was inspected with the aid of a microscope.

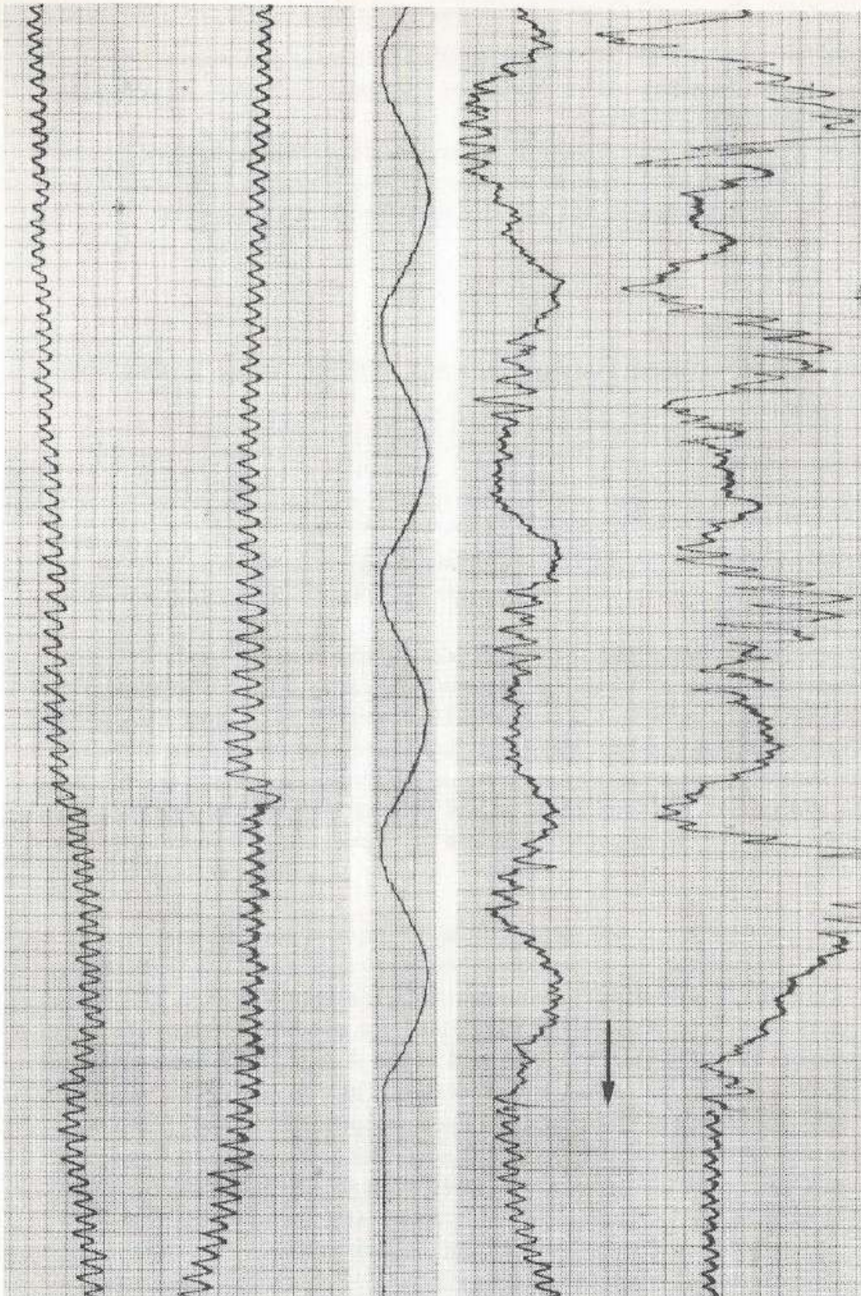
9b). OBSERVATIONS FOLLOWING UNILATERAL TOTAL LABYRINTHECTOMY

We considered ten cases in which movements of both eyes were recorded following a unilateral total labyrinthectomy. We shall consider two aspects:

a. The nystagmus provoked by the unilateral labyrinthectomy;
b. The effects on the compensatory eye deviation following unilateral labyrinthectomy.

Not only have we observed the effects of labyrinthectomy on the two eyes separately during rotation but also the modulating effect of inverting the rotation from clockwise to counter-clockwise and vice versa. Since the responses provoked by unilateral labyrinthectomy have been adequately studied in the stationary positions (supine, prone and both lateral sides, Bos 1962, Bos and Philipszoon 1963 and Jongkees and Philipszoon 1964) we can limit our observations to the responses provoked by a barbecue rotation at constant speed.

a. On the nystagmus: We measured the influence of the barbecue rotation on the spontaneous nystagmus in both eyes separately. The spontaneous nystagmus recorded from the unoperated side was more intense. This could be judged from both the amplitude and the maximal speed of the slow phase. The amplitude and the speed of the slow phase of the nystagmus appeared to be modulated during rotation. This was noticed for both eyes (fig. 26). Maximal amplitude and maximal speed of the slow phase were measured when the rabbit moved through the prone position. Nystagmus was suppressed when the rabbit moved through a supine position, in fact, in some cases, it even disappeared. It seems as if the intensity of the nystagmus waxed and waned as the rabbit occupied different positions during the consecutive parts of the rotation (fig. 27 E, F, G and H). When we compare in this figure the intensity of the nystagmus in the supine position: first, when the rabbit is stationary and second, during rotation, we notice that during rotation the nystagmus is markedly less intense and, as we have already mentioned, it even disappeared. This suggests that the rotational



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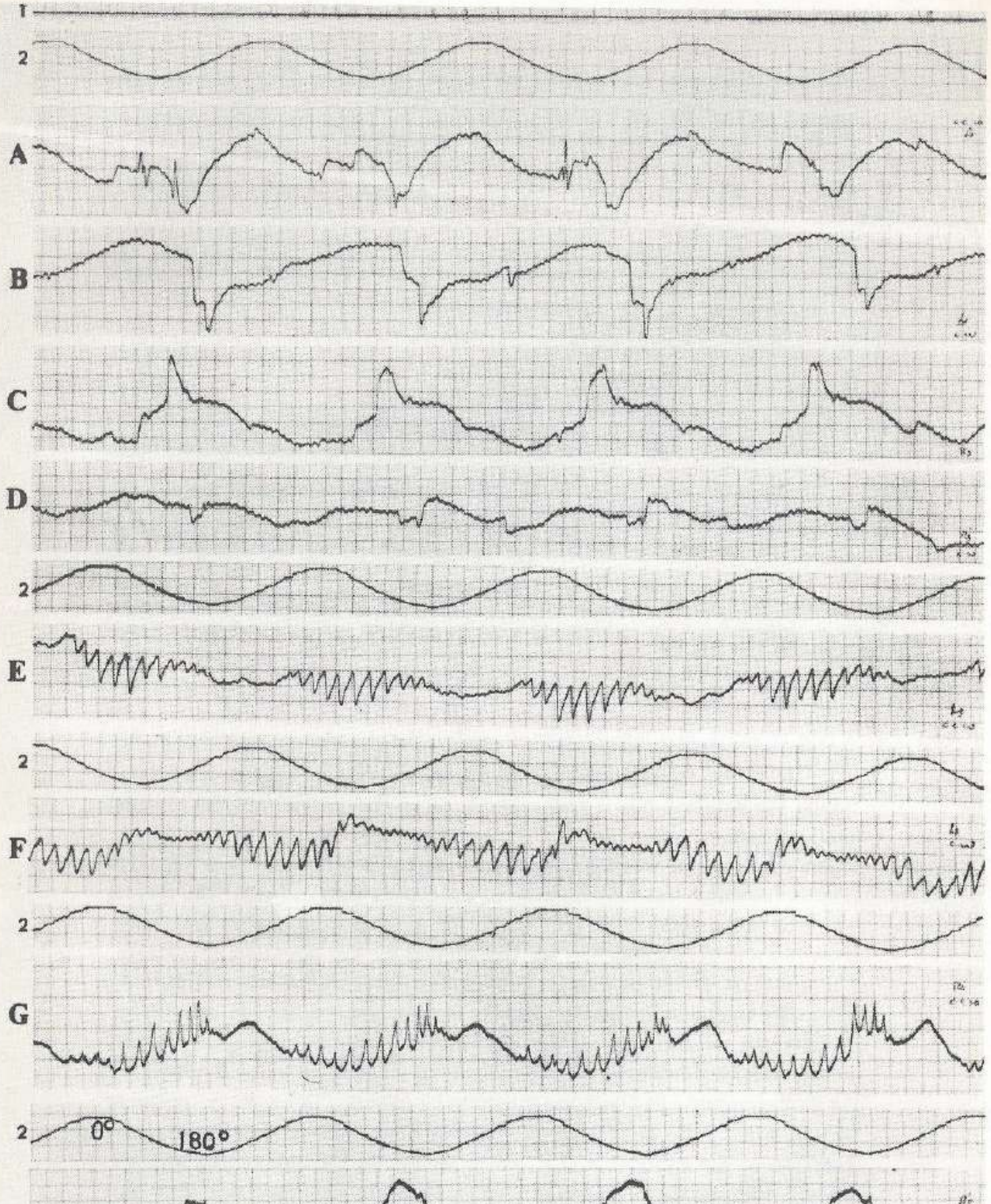

Fig. 26.

Spontaneous nystagmus provoked by unilateral labyrinthectomy on the left side.
A and B = Left and right eye responses (horizontal leads).
C and D = Left and right eye responses, modulated by a clockwise barbecue rotation.
1 = Position of the animal; uppermost point: prone position.

Fig. 27.

Recording of the eye responses following a labyrinthectomy on the left side. Pre-operative (A, B, C and D) and post-operative recordings (E, F, G and H) during constant rotation.
1 = time in seconds; 2 = barbecue stimulation.
A = recording from left eye (counter clockwise)
B = recording from left eye (clockwise)
C = recording from right eye (counter clockwise)
D = recording from right eye (clockwise)
E = recording from left eye (counter clockwise) following a left-sided labyrinthectomy.
F = recording from left eye (clockwise) following a left-sided labyrinthectomy.
G = recording from right eye (counter clockwise) following a left-sided labyrinthectomy.
H = recording from right eye (clockwise) following a left-sided labyrinthectomy.
The above recordings were from the horizontal leads.
One notices that: a) The amplitude of the slow eye movement on the unoperated side (right eye) has increased which is especially noticeable when the rotation is clockwise (H).
b) The polarity of the nystagmus provoked by a left-sided labyrinthectomy changes in accordance with the direction of gravity (see H). The post-operative amplitude of the eye deviation on the operated side is smaller than the pre-operative value (A and B).

motion adds to this "suppressive" effect of the nystagmus in certain positions, (e.g. the supine position). Not only was the nystagmus modulated during the rotation but it changed also when the direction of the rotation was inverted.

When the rotation was clockwise the nystagmus provoked by a left-sided labyrinthectomy was more intense in the eye on the right side. The reverse was true for a right-sided labyrinthectomy. This implies that the modulating effects of the rotation are determined by the direction of rotation. The direction of the nystagmus provoked by a unilateral labyrinthectomy is usually with its fast phase towards the unoperated side. In our experiments eight of the ten rabbits showed a direction-changing nystagmus during constant barbecue rotation. (See fig. 27 and 28.) The direction of the nystagmus inverted with the direction of gravity. Although the response was recorded from both eyes we can only state with confidence that the direction of the nystagmus changed in the eye on the unoperated side. We can say nothing about a possible inversion on the operated side since the movements are too minute and rapid. It is difficult to differentiate between nosemovements and nystagmus of a small amplitude superimposed on a sinusoidally changing eye movement. Only large differences can be judged as proof.

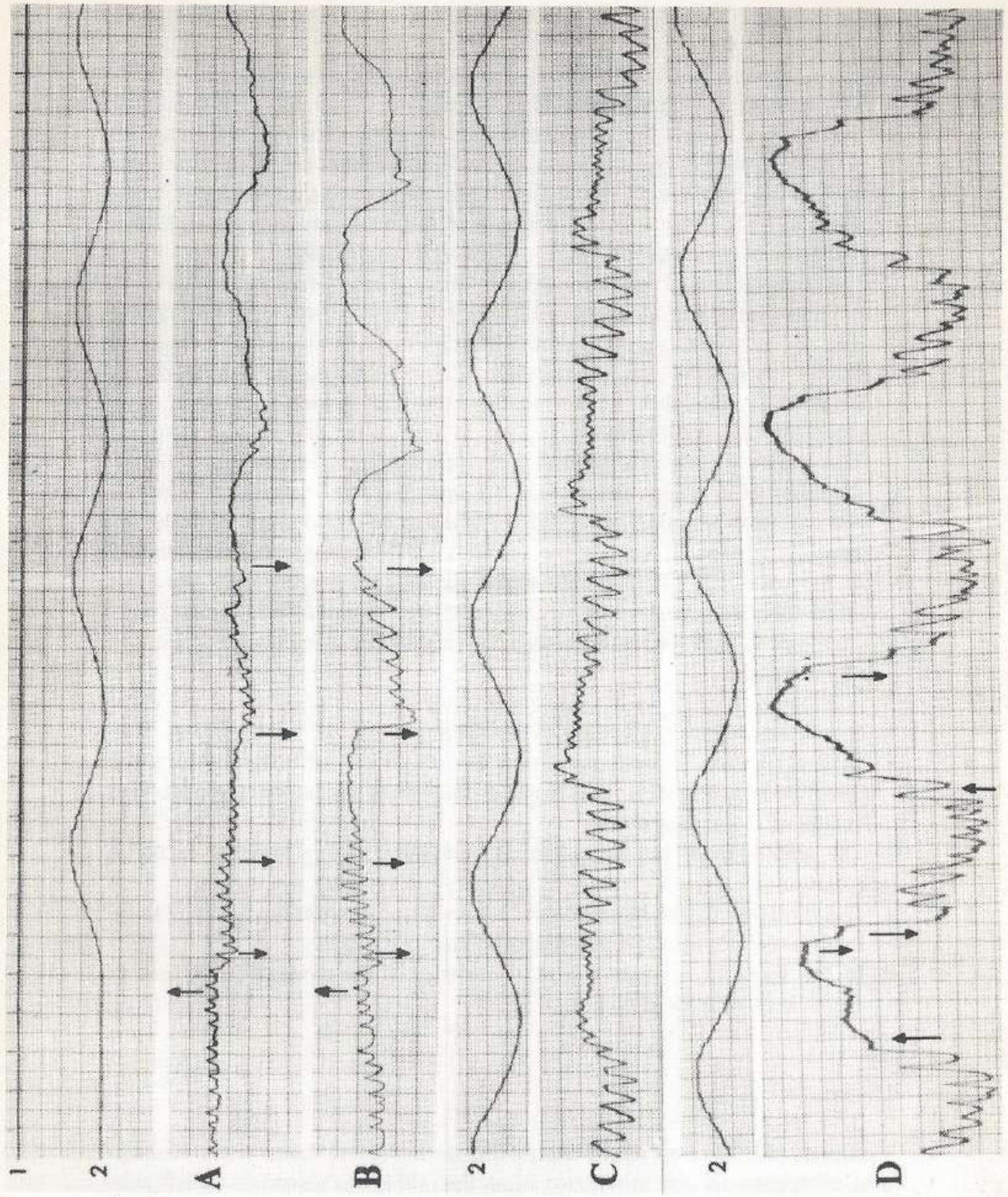

Fig. 28.

Modulation of different forms of nystagmus during a barbecue rotation. (Horizontal leads).
2 = barbecue rotation. (c.w.)
A and B = nystagmus of the left and right eye provoked by alcohol intoxication.
C and D = nystagmus of the left and right eye provoked by unilateral labyrinthectomy on the left side.

b. On the eye deviation: In the case of a normal animal both eyes deviate rhythmically during barbecue rotation, each with a certain amplitude (e.g. fig. 27 A, B, C and D). When unilateral labyrinthectomy is performed the amplitude of the eye deviation on the unoperated side is increased and reaches in some cases as much as double the pre-operative value. On the operated side, though, the amplitude of the compensatory eye deviation decreases in comparison with its pre-operative amplitude.
   Effects determined by the direction of the rotation (i.e. clockwise or counter-clockwise) were noticed in the same way as for nystagmus. In the case of a left-sided labyrinthectomy the amplitude of the slow eye deviation on the unoperated side, provoked by a clockwise rotation, was markedly bigger than when the rotation was inverted. The opposite is true for right-sided labyrinth extirpation.
   This seems to imply that each labyrinth has a preference for a certain direction of rotation. Because on the operated side the amplitude of the eye deviation was smaller this effect was not as pronounced as on the unoperated side. In all respects the horizontal and vertical recordings behaved in the same way. This implies that unilateral labyrinthectomy does not influence the inclination of an eye movement with respect the electrodes. (Remember that we cannot assess any rotational component of the eye movement.)

In conclusion we give a summary of our findings:

a. During rotation at constant speed the amplitude of compensatory eye deviation and of nystagmus is bigger in the eye on the unoperated side than in that of the operated side.
b. The amplitude of the nystagmus is modulated during constant barbecue rotation.
c. The direction of the rotation (i.e. clockwise or counter-clockwise) can influence the amplitude of eye deviation and nystagmus.
d. In the majority of cases the sense polarity of the nystagmus changed in accordance with the direction of gravity.

Discussion

Versteegh (1927) resected the right utricular nerve and found a maximal vertical compensatory eye movement when the rabbit was placed on its left side. When it was placed on its right side no compensatory eye movement was noticed. Cawthorne, et al (1942), performed caloric tests on patients after a surgical unilateral labyrinthectomy for vertigo due to Ménière's disease. The caloric reactions of the unoperated ear were tested post-operatively. Their cases revealed "a striking and well-systematized variety of changes in the normal relationship of the two reactions, consisting of an increase of the hot and a concurrent diminution of the cold responses and a consistent marked directional preponderance of caloric nystagmus to the side of the intact ear". In the course of time the intact ear underwent a considerable degree of restoration to the normal. Fluur (1961) reported on the post-operative findings of six unilaterally labyrinthectomized patients. He irrigated the healthy ear with warm water and found as a result of the operation an increase in the duration and frequency of the nystagmus in all ten patients. Walsh (1960) tested humans who had lost the function of one labyrinth, to a linear acceleration. The sensation seems to be increased when the patients were lying on the side of the intact labyrinth.

He ascribes this to the participation of the saccule which responds to a shearing force parallel to the main part of its macula. Jongkees (1966) performed a unilateral labyrinthectomy on rabbits. Hereafter the animals were tested on the parallel swing. They were a.o. placed with the operated side underneath. The eye deviations provoked by linear acceleration were of greater amplitude than pre-operatively when the same ear was facing downwards. The results of our experiments are similar to the findings of the above authors, in the sense that when the remaining otolith organ is stimulated with the parallel swing or the barbecue rotation it gives a greater response than when both sides are intact. It appears that when both labyrinths are intact, they exhibit an inhibitory effect upon one another. The fact that the nystagmus following an unilateral labyrinthectomy is changed in direction and modulated in magnitude by the barbecue rotation can only be explained on the basis of an otolith influence. Our results do not wholly support the view that the nystagmus resulting from a peripheral lesion always beats in the same direction (Ewald), because during barbecue rotation the nystagmus can change its polarity.

We can now compare the modulating influences of the otoliths on different forms of nystagmus, viz. p.a.n. and the nystagmus provoked by unilateral extirpation. We then notice a clear difference between these two. In fig. 28 it is seen that p.a.n. is to a great extent suppressed during the barbecue rotation. The suppression is only fully attained after the barbecue rotation has completed a few rotations. On the other hand, the nystagmus provoked by extirpation of one labyrinth is increased during barbecue rotation, and it remains present. Hence there are at least two types of modulating effects, viz. a transitory and a stationary one. In the case of a unilateral labyrinthectomy the lesion is definitely peripheral, hence the cause of the resulting nystagmus may be named a peripheral one. The modulating effect here is of the stationary type and may include the inversion of polarity. The exact machanism of alcohol nystagmus is not yet clear, but according to the above results it seems to be not of peripheral origin. In this case the modulation is transitory and it does not involve a change of polarity. Our conclusion does not agree with the views of Money and Scott (1962); Nito, et al (1964) and Money, et al (1965), that p.a.n. originates solely from the canal system. If this were the case there is no reason why the modulating pattern resulting from barbecue rotation should not be the same for both the nystagmus provoked by a one-sided extirpation and p.a.n.

9c). UTRICULAR STIMULATION. (ELECTRICAL AND MECHANICAL.)

It is known that linear accelerations can give nystagmus (Jongkees and Philipszoon 1962). However, it is not known whether electrical or mechanical stimulation of the utricular macula or it's nerve leads to nystagmus or whether electrical stimulation influences an already present nystagmus. Versteegh (1927), Jongkees (1949), Sullivan et al (1957) denied any development of nystagmus by direct mechanical stimulation of the otolith system. On the other hand Ulrich (1935) provoked nystagmus by direct stimulation of the otoliths with a human hair.

From the data of other authors (see lit. rev.) we cannot come to a definite conclusion as to what the effects of artificial stimulation on the utriculus or its nerve are. In our approach toward sectioning of the utricular nerve we encounter a phase where stimulation of the nerve is very easy.

Materials and Procedure

We used a series of seven rabbits of which five were successful. In two the pars utricularis was damaged during the stimulation because of movements of the animal. The operational approach was the same as earlier described.

A steel electrode was held in position by a micromanipulator (made by Narishige, Japan) so that either the utricle or its nerve could be stimulated separately. A Grass stimulator was used to deliver the electrical impulses and was set at 0.5 - 0.8 V open-circuit voltage. The pulses lasted 0.1 second and were given at the ratio of 5 per second. After stimulation of the macula and the nerve, the electrode was moved mechanically up and down on the nerve and the macula over a distance of 100 μ. This allows us to separate electrical from mechanical stimulation.

Results

After the anaesthesia had worn off sufficiently we started our recordings. The salient features of the electrical stimulation was as follows.

a. No nystagmus was observed by direct observation.
In two animals an eye deviation was noticed on the nystagmogram while the rest of the examined animals exhibited a rotatory movement ot the eyeballs which was not recorded on the nystagmogram. Mechanical pressure on the utricular nerve did not provoke any response. When we moved the electrode up and down the utricular macula we observed an intense nystagmus in both eyes. Such a movement simulates in exaggerated form a linear acceleration. After these experiments we destroyed the utricle and the canals, and the typical nystagmus followed, beating with the fast phase to the normal side. We now stimulated the utricular nerve stump. In three animals a suppression of the nystagmus followed. This suppression lasted till a few seconds after the stimulus ceased.

Discussion

From the results of our experiments we conclude that two factors are of value namely: i) that nystagmus beats cannot be generated by direct electrical or mechanical stimulation of the utricular nerve and ii) that with a minimal pressure on the utricular membrane an intense nystagmus results. We may regard the latter most probably as an otolith reaction but it may be due to a mechanical displacement of endolymph with a resultant cupula deflexion (outside physiological bounds) as well.

9d). SELECTIVE LABYRINTHECTOMY

In order to examine the relationship between the otoliths and the nystagmus provoked by linear acceleration, we tried to remove parts of the labyrinth. Surgical intervention on the labyrinth makes it possible to prove that the semicircular canals do not respond to a linear acceleration. It is, however, very difficult to perform selective operations on the otolith system without damaging other parts of the labyrinth, i.e. the canals. It is impossible to state with confidence that the functional alteration of the labyrinth can be confirmed histologically (James, personal communication). For this reason we did not rely on histological techniques. We intended to examine the effects of the otoliths by way of physiological recordings. In how far the otoliths are responsible for nystagmus can be found out by a step-by-step elimination of various sub-organs: first the saccule and then the utricle. Every step of the operation was checked with rotation tests about a vertical as well as a horizontal axis, hence a light anaesthesia is mandatory.

Materials and procedure

Our serie consisted of more than fifty rabbits of which only seven were classified as successful on both sides. The labyrinth function of each animal was evaluated pre-operatively by a torsion-swing, a parallel-swing and a barbecue test.

The approach to the inner ear has already been described. To facilitate the sectioning of the utricular nerve, we tried a few techniques with different degrees of success. When the utricular nerve is touched with the hooklet, it presumably gives an intense stimulation, which causes the animal to start struggling. This might result in a tear of the limiting membrane or damage of the nerve of the lateral semicircular canal, and this would eventually lead to a failure of the operation. The failure is indicated by a spontaneous nystagmus beating to the normal side, the same as in the case of a unilateral total labyrinthectomy.

For this reason we proceeded either by cocainization of the utricular nerve with a few drops of a 5% solution or by paralyzing the animal with flaxedil 1-2 mg/kg of body weight. After removing blood clots and perilymph leaking from the cochlea, the utricular nerve was hooked and cut through under the microscope. The hooklet was made in our workshop and was not bigger than 100 micron. The wound was flushed with a penicillin solution and closed. Penicillin was administered i.m. for five days post-operatively.

Results

Spontaneous nystagmus resulting from utricular nerve sectioning alone was not seen in the successful cases. This coincides with the results of Versteegh (1927), Jongkees (1950), Sullivan, et al (1957) and Sasaki (1963). But if the limiting membrane or the nerve from the lateral semicircular canal was damaged, spontaneous nystagmus appeared. The nystagmus beats to the normal side, the same as in the case of a unilateral labyrinthectomy. Fernandez, et al (1959) reported spontaneous nystagmus after the sectioning of the utricular nerve. This we must attribute to damage of the canal system as in our cases which we classify as being non-successful.

Directly following the sectioning of the utricular nerve we noticed a tremor of the eyelid, more pronounced in the upper one on the operated side. In some cases the mambrana nictitans participated. The eyeball, however, stood still. This eyelid tremor is clearly recorded by the nystagmograph and can easily be mistaken for eyeball tremors (Hamersma 1957).

Sirabe, et al (1965) stimulated the otoliths by centrifugal force and in this way provoked a vertical eyeball tremor (no nystagmus). They ascribed it to "eye-muscle cramps", which might be an otolith reflex according to the authors.

It might have been only an eyelid tremor and not an eyeball tremor. This confirms the necessity for direct observation.

The disturbance of equilibrium after bilateral otolith destruction was characterized by a swaying of the head from left to right and vice versa in a horizontal plane, abduction of the hind limbs and a broad gait. This disorder appeared in all the animals with a selective bilateral loss of utricular function, as well as in animals with a bilateral total labyrinth destruction. It seems that this unstable condition is brought about by the loss of otolith function (Jongkees 1950). Before we proceeded to the barbecue rotation we tested the reaction to rotation and linear stimulation. The post-operative cupular responses provoked by the torsion swing were not identical to the pre-operative recordings fig. 29. The reason for this might be a minute tear in the limiting membrane or a bleeding in the endolymphatic space, such as were observed in some cases in post-mortem examination (Miehlke 1955). This change of torsion-swing response might on first sight, be attributable to disappearance of otolith influence. But this is very unlikely since we encountered animals in which torsion-swing recordings were nearly normal. On the parallel swing no trace of reaction was ever noticed.

During barbecue rotation the only responses were those provoked by the rotatory acceleration resulting in a transitory nystagmus. This is also regarded as a proof of the functionality of the vertical canals (fig. 30). During constant rotation we noticed no response at all.

Discussion

Benjamins and Huizinga (1927 and 1928) removed the pars superior of the labyrinth (utricle and canals) on both sides in pigeons and noticed that the counter-rolling of the eyes remained intact. If they removed the pars inferior (saccule, cochlea and lagena) counter-rolling was no longer observed. By using the same principle of elimination, Philipszoon and v.d. Laarse (1962) also came to the conclusion that the compensatory eye movement originates in the otoliths. They eliminated the saccule and cut the utricular nerve on one side. The contralateral side was destroyed.

We are convinced that our technique provides sufficient accuracy to conclude that both the compensatory eye movements and the concomitant nystagmus during barbecue rotation are provoked by the otoliths. Here we see that the canals do not respond to linear accelerations and that otolith stimulation can provoke nystagmus. Although on incorrect grounds, Borries in 1922 was the first to mention the otolith-ocular reflex arch. Many years later, Jongkees and Philipszoon (1962) proved that a linear acceleration which is the appropriate stimulus for the otoliths can provoke nystagmus.

Now that a more positive proof of an otolith-ocular reflex arch exists, we get a better insight into the origin of positional nystagmus. We do not suggest

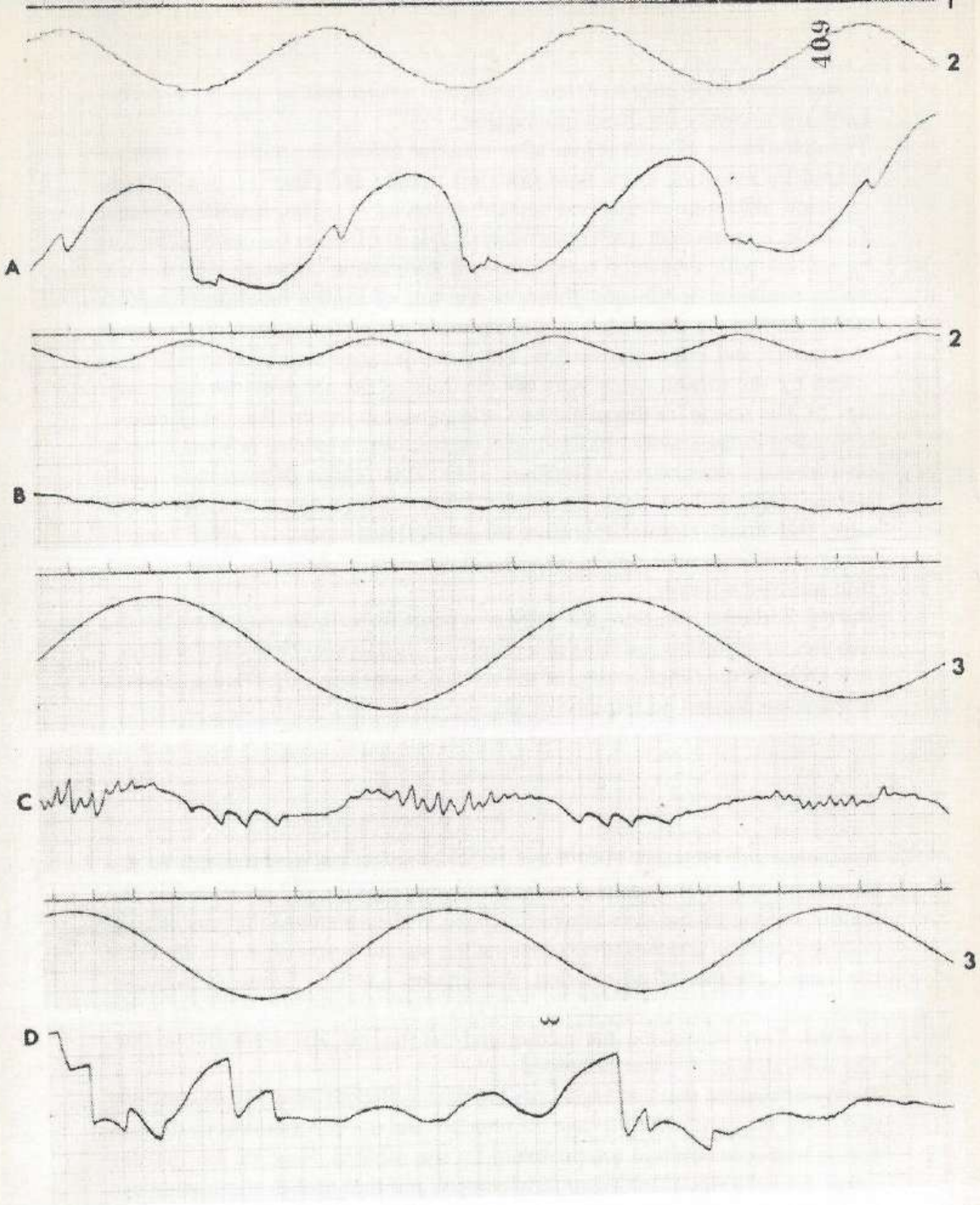

Fig. 29.

Labyrinth responses following a selective labyrinthectomy on both sides:
1 = time in seconds.
2 = barbecue stimulation.
3 = torsion-swing stimulation.
A = pre-operative response to the barbecue stimulation.
B = post-operative response to the barbecue stimulation.
C = pre-operative response to the torsion-swing stimulation.
D = post-operative response to the torsion-swing stimulation.

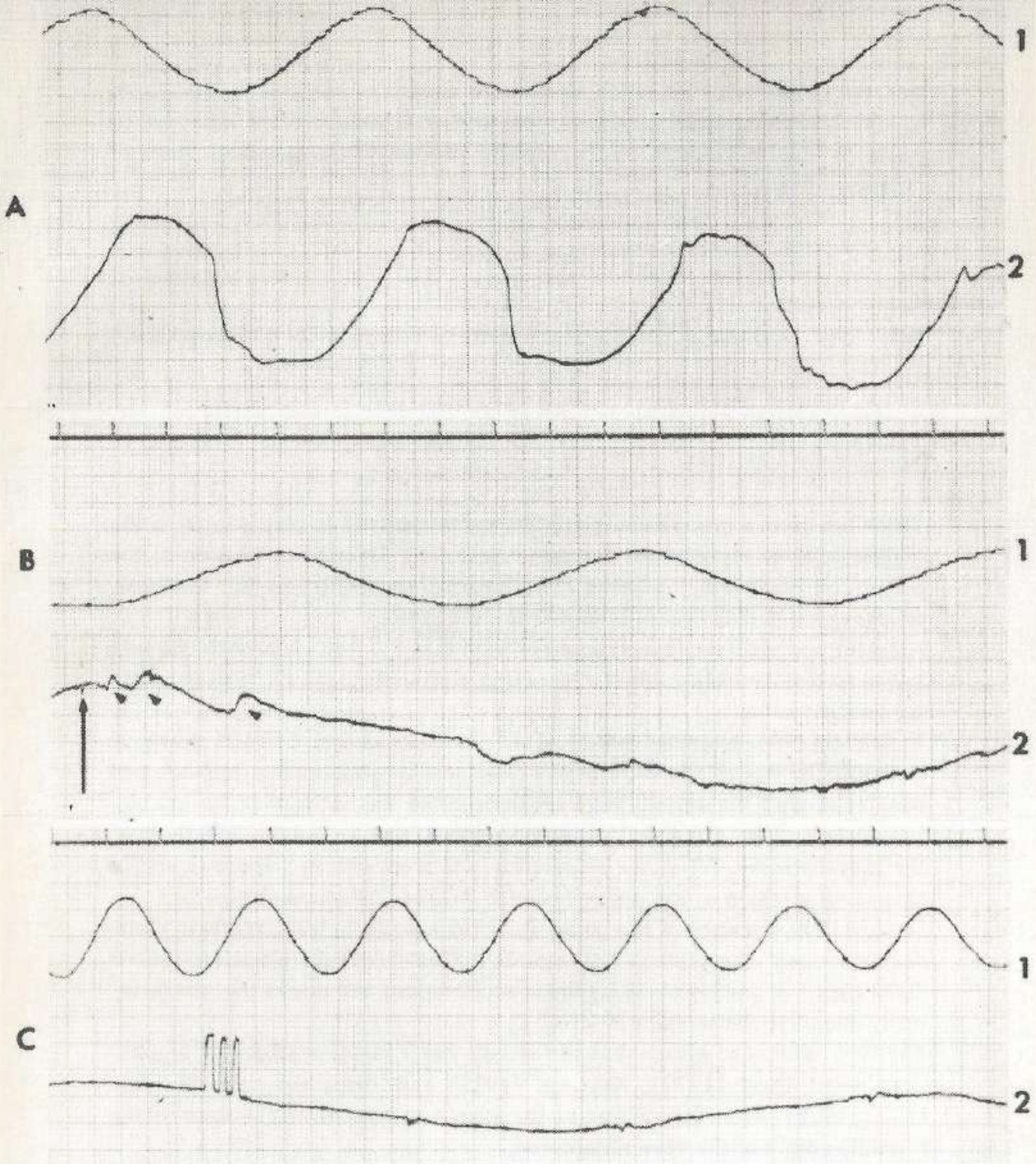

Fig. 30.

Labyrinth responses following a selective labyrinthectomy on both sides:
A1 = barbecue stimulus. (B1).
A2 = pre-operative response.
B2 = post-operative response to the barbecue stimulation.
C1 = parallel-swing stimulus.
C2 = negative response to linear accelerations. The 3 squares are calibration waves which indicates that 500 μ V = 1 cm on the vertical axis.
The arrow indicates the start of the barbecue rotation. A few nystagmus beats provoked by the acceleration are seen in 2b.

that the physiology of a rabbit is the same as that of humans, neither do we intend to exclude other forms of positional nystagmus, but we only want to point to the importance of the otoliths as one of the possible causes of positional nystagmus.

9e). SOME CONSIDERATIONS ON THE FUNCTION OF THE SACCULE

Introduction

There has been a time that the saccule was considered to play no part in the maintenance of equilibrium but rather to have a function in relation to the perception of sound. Versteegh (1927) found no changes in the vestibular reflexes after destruction of both saccules in rabbits.

Ashcroft and Hallpike (1934) demonstrated that if a frog's labyrinth was subjected to low-frequency vibrations, action potentials could be obtained from the saccular nerve.

V. Békésy (1935) subjected individuals to loud sound beats, 110-120 dB above threshold. He was able to show head movements synchronous to the beats and concluded that the stimuli were transduced via the otoliths of the saccule. Löwenstein (1949) recorded electric impulses from an isolated labyrinth of the thornback ray. When the preparation was submitted to vibrations, and to changes of position action potentials were recorded via micro-electrodes.

Sasaki (1960) mentioned in a paper that "the saccule, at least, reacts to vibration and sound". Jongkees (1950) regards the low-frequency vibrations (below 1000 c.p.s.) as quickly-changing linear accelerations and thinks that the latter really stimulate the saccular otolith.

The first authors to notice that the saccule has a function related to equilibrium were Quix (1922), Huizinga (1925) and Benjamins and Huizinga (1927, 1928). After destruction of the saccule in pigeons, the counter-rolling ("raddraaiing") of the eyes disappeared.

Hasegawa (1937) destroyed the saccule in guinea pigs and frogs and noticed the disappearance of responses to a dorso-ventral linear acceleration. Lorente de Nó stated (1933): "An accoustic function of the saccule cannot be accepted because although it has connections with the centres and pathways involved in the regulation of equilibrium, it has no connection with the pathways and centres involved in hearing". Adrian (1943) relayed signals from the vestibular receptors in the brain-stem of cats. If pressure in the saccular otoliths was changed by the action of linear acceleration the activity of the receptors changed too. Groen and Jongkees (1946) held the view that the saccule has a possible equilibrium function. Jongkees (1949) performed a series of experiments on rabbits concerning the saccule. After the destruction of one of the two saccules, the rabbits reacted normally to thermal and rotatory stimuli. When both were destroyed the reactions to linear accelerations as provoked by a parallel-swing (·6 g) were diminished. When a steel ball was brought into the vestibule and by way of a magnetic field pressed against the intact saccule the head of the rabbit moved towards the magnet and the reaction to a linear acceleration in a bi-temporal direction was much increased. The author concludes that the saccule has a vestibular function and reacts to linear acceleration. Watanabe (1959) and later Sasaki (1963) subjected humans to linear accelerations in different directions. They are of the opinion that the otoliths of the saccule are stimulated by linear accelerations. Nevertheless "both otolith systems have a mutual and duplicate or subsidiary function". Owada, et al (1960) resected the saccular nerve in rabbits and found that the compensatory deviation of the eyeballs is influenced by the saccule. When pressure is applied on the otolith of the saccular macula, the nystagmus on the same side is inhibited.

Walsh (1960) argued that the saccule participates in the responses provoked by the parallel swing. Bos et al (1963) confirmed his findings. Jongkees and Philipszoon (1962, 1963) found that the compensatory eye movements completely disappeared after destruction of both labyrinths but remained as long as one otolith organ, either saccule or utricle, is still present. Shirabe, et al (1965) performed caloric tests in humans. By means of centrifugal force the saccular otoliths were "pressed" upon their macula which resulted in a homolateral decrease of nystagmus. Jongkees (1966) performed experiments on rabbits which were subjected to a parallel-swing stimulus. When only either one saccule or one utricle was present the compensatory eye movements could still be provoked. The reason why Versteegh could not find a definite saccular function in the vestibular field may be due to the fact that the utricle overrules the saccule or that the function of the destroyed saccule is taken over by the utricle (Jongkees 1949). Versteegh also did his experiments in the era that the otoliths were thought to react to static and the canals to dynamic stimuli. He found that reactions to linear movements (Sprungbereitschaft, lift reaction) were changed but attributed this effect as being "dynamic" to concomitant lesions to the semicircular canals.

Reviewing the literature we may conclude that there are many arguments to support the theory that the saccule possesses a vestibular function. For this reason we tried to repeat the experiments of Versteegh (1927) with a little modification added to his technique. Instead of destroying only the saccule (pars inferior) and subjecting the animal to various vestibular tests to observe any alteration in the labyrinth function, we performed the sequence of the operation in reverse. The utricular nerve was severed whilst the saccule was left intact (on both sides).

Execution of the experiments:

We tried to cut the utricular nerve without damaging the saccule. If the saccular membrane was ruptured by accident the operation was changed and we cut the utricular nerve for other experiments (see previous chapter). If the saccular membrane remained intact we had a case with an anatomically intact pars superior (except that the utricle is without nerve connections and therefore non-functional) and a intact saccule. Since this is a very difficult procedure we could only regard three cases of fifty-five as a success. In these cases the operation was performed on both sides. We also performed post-mortems to verify the results of the surgical interventions. Parallel- and torsion-swing tests and lastly a barbecue-rotation test were performed in order to assess the responses and to confirm the functioning of the canals. Test on the parallel swing demonstrated a compensatory eye movement when the linear acceleration was applied from one side to the other. The highest amplitudes were recorded in one or the other side position. Nystagmus beats were also noticed at about the peak of the compensatory eye movements but these were small and could not easily be differentiated from the rabbit's nose movements, see fig. 31, C and D.

Observations:

When the saccule alone was destroyed and the utricle was left intactand functioning, no alteration of the labyrinth responses as provoked by the barbecue rotation, compared to intact animals, were noticed. This coincides with the general results of Versteegh (1927), Jongkees (1949) that it appears as if the function of the saccule is overshadowed by the intact utricle.
When animals with destroyed utricular nerves and only the saccules functionally intact were tested, we noticed a weak response provoked by the barbecue stimulation (clockwise and counter-clockwise), (fig. 31, C and D). The number of experimental rabbits was too small to draw a conclusion as to whether there exists a statistically significant difference between the amplitude of the deviation of the left and the right eye provoked by a clockwise or counter-

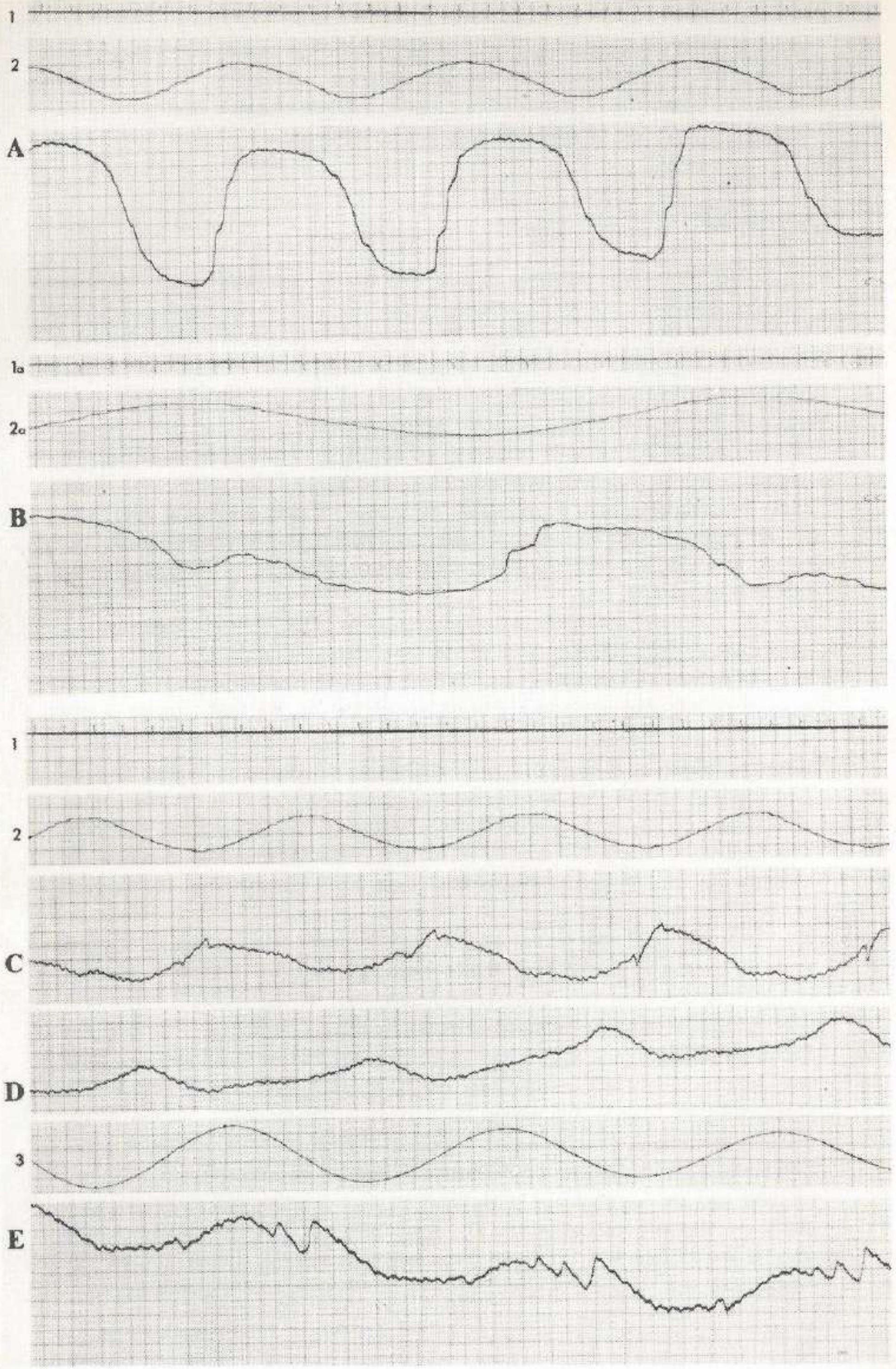

Fig. 31.

Labyrinth responses following utricular nerve sectioning (left and right); the saccules on both sides were left intact.
1 = time in seconds.
2 = barbecue stimulation (paperspeed 1 cm/sec.).
2a = barbecue stimulation (the paperspeed was faster, 2.5 cm/sec.).
A = horizontal lead of left eye (clockwise).
B = horizontal lead of left eye (counter-clock wise).
C and D = post-operative recording from left eye.
C = clockwise and D = counter-clockwise. Both are horizontal leads.
E = post-operative torsion-swing responses to evaluate the function of the lateral canals.

clockwise barbecue rotation. The amplitude of the eye movement was markedly reduced in comparison to the pre-operative values (fig. 31 A and B). Weak nystagmus beats were noticed; the amplitude changed during the rotations. The direction of the nystagmus did not change.

Discussion

Although our results strongly suggest that the saccule possesses a vestibular function it seems to be by far inferior to the utricle in its reaction to barbecue rotation and in parallel-swing test. This might be the reason why its function has been frequently overlooked by some investigators. It may also be that already the operation upon the inferior part of the labyrinth in itself so far damages the saccule, that it becomes subfunctional.

These findings corroborate the views of Benjamins and Huizinga, Hasegawa, Lorente de Nó, Adrian, Jongkees, Bos, Jongkees, Philipszoon and Walsh that the saccule must be regarded as a part of the vestibular labyrinth.

In our earlier results regarding the post-rotatory nystagmus provoked by barbecue rotation, we notice a difference in the responses of both eyes in the lateral position (fig. 18).

The post-rotatory nystagmus in the lower eye was more intense. The frequency of beats and the maximal speed of the slow phase was markedly larger. If we base ourselves on the above assumption, (that the saccule has a vestibular function), this phenomenon can easily be explained. We first have to review the orientation of the otoliths in relation to their maculae in space. In the prone position the utricular otoliths are resting on top of their sensory cells. The saccular otoliths are hanging from the lateral side of their maculae. When the rabbits occupy side positions the otoliths of the utricle hang sideways. The otolith of the upper saccule rests on its macula. In supine position the utricular otoliths hang perpendicularly from their maculae and the saccular otoliths hang sideways.

The angle between the planes of the saccular and utricular macula is more than 90°, approximately 110° (Quix 1925, James 1968 personal communication) and can even vary from animal to animal. If the rabbit is stopped at angle of 90° in relation to gravity (lateral position) the saccule occupies the following position: the upper one approximately 20° declined and the lower one approximately 20° inclined to the horizontal plane. According to the shearing-forces theory this would be near to a maximal stimulation of the macular epithelium (Breuer 1891; Ulrich 1935; Von Holst 1950; Walsh 1960; Colebrander 1964; Békésy 1966; Beerens 1968 in contrary to Quix 1923 and Magnus and De Kleijn 1924 who believed that pressure and pulling respectively are the effective stimuli). The lower saccule would be more sensitive since it hangs free and does not press upon its macula. From this we can understand why the lower eye gives a greater response in a lateral position.

SUMMARY

It is known that nystagmus can be provoked by stimulation of semicircular canals which are sensitive to angular accelerations. However, it is not clearly established which part the otolith system (utricle and saccule) plays in the formation of nystagmus when it is stimulated by linear acceleration.

To study this problem we applied a series of different combinations of stimuli to normal rabbits.

We activated the labyrinths by a rotation about a cephalo-caudal horizontal axis (commonly called barbecue rotation). This offered us a possibility to separate cupular and otolithic responses from one another. Additionally the modulating effects of both sub-organs on one another could be investigated. The response to a constant barbecue rotation can be divided into two components, namely a slow sinusoidal eye movement which lasts as long as the rotation is present and a real nystagmus. These responses touch on the basic principles of labyrinthology for the eye deviation appears to be an otolithic response and the concomitant nystagmus too. This implies that the semicircular canals are not the only generators of nystagmus. When the eye is deviated to an extreme position (in this case by otolith activity), the quick or correction phase of nystagmus is provoked (Alexander's law 1929). This view was confirmed in the next set of experiments.

The barbecue rotation was perturbed by a rotation about a vertical axis; the latter was non-uniform so as to study the influence of rotational acceleration on the barbecue response. The reaction patterns to both types of stimulation remained independant to a fair degree. This shows that two different sub-organs, viz. the otoliths and the canals, are responsible for the two reaction patterns. It shows as well that the canal system is able to modulate otolith responses.

In addition we also tested the effect of fentanyl and alcohol upon the labyrinth reflexes as provoked by barbecue rotation. Fentanyl appeared to suppress the quick phase of nystagmus, whereas the peripheral organ remained active as judged by the slow eye movements. In the case of alcohol we came to the conclusion that positional alcohol nystagmus (p.a.n.) is of central origin and is constantly present but modulated by the otoliths depending on the orientation in relation to the direction of gravity.

From the results of an unilateral labyrinthectomy it appears that when both labyrinths are intact, most often inhibitory influences upon one another are present. The direction of the spontaneous nystagmus following unilateral labyrinthectomy is changed in accordance to the direction of gravity during barbecue rotation. This modulation of nystagmus can be attributed to the otoliths of the unoperated side.

As a further check we stimulated the utricle and its nerve mechanicallv and

electrically. In the successful cases we could not provoke nystagmus by electrical stimulation of either the utricle or its nerve. By means of mechanical stimulation of the utricular macula we could indeed provoke nystagmus *whilst cupular activity could be excluded.*

Following a partial labyrinthectomy on both sides in which the utricular nerves were severed, the saccules destroyed, and the canals were left in tact, the slow eye movement and the concomitant nystagmus disappeared. This proves that both the slow eye movement and the concomitant nystagmus originates from the otoliths. (The integrity of the canals is confirmed by a torsion-swing test). It also proves that the canal system is not gravity-sensitive, *nor can it be regarded as a linear accelerometer at all.*

The function of the saccule was long regarded as being non-vestibular. From our results we conclude that the saccule possesses a vestibular function. It appears that the saccular function is normally overshadowed by utricular function. This might be one of the reasons why so many authors in the past have overlooked the saccule as a vestibular organ.

In this work we proved that there exists at least two different reflex arches viz: the cupula-ocular and the otolith-ocular reflex arches. Both can be regarded as feedback systems which handle different forms of accelerations, either angular or linear. They operate more or less independantly but some modulating effect of one on the other (and vice versa) can clearly be demonstrated.

SAMENVATTING

Het is bekend, dat door prikkeling van de halfcirkelvormige kanalen, die gevoelig zijn voor hoekversnellingen, nystagmus kan worden opgewekt. Welke betekenis het otoliet-systeem (utriculus en sacculus) heeft voor het ontstaan van nystagmus bij prikkeling door rechtlijnige versnellingen is echter niet duidelijk.

Om dit probleem te bestuderen hebben wij normale konijnen aan een reeks prikkels in verschillende combinaties blootgesteld. Door middel van draaiing om de lengteas van het proefdier in het horizontale vlak (gewoonlijk "barbecuerotatie" genoemd) werden de labyrinthen geprikkeld, hetgeen ons een mogelijkheid bood de reacties van de cupulae en de otolieten van elkaar te scheiden. Tevens konden aldus de regulerende effecten van beide sub-organen ten opzichte van elkaar worden onderzocht.

De reactie op een constante barbecue-rotatie kan in twee componenten verdeeld worden en wel in een langzame, sinusoidale oogbeweging, die duurt zolang de rotatie aanhoudt, en een echte nystagmus. Deze reacties raken de principes van de labyrinthologie, want niet alleen de oogbeweging maar ook de begeleidende nystagmus blijkt een otoliet reactie te zijn. Dit houdt in dat de halfcirkelvormige kanalen niet de enige verwekkers van nystagmus zijn. Wanneer het oog tot een zekere grens op zij gewend wordt (in dit geval door otoliet werking) wordt de snelle oftewel correctiefase van de nystagmus opgewekt. (Wet van Alexander 1929). Dit standpunt werd in de volgende reeks experimenten bevestigd:

De barbecue rotatie werd uitgevoerd in combinatie met een draaiing om een vertikale as; de laatstgenoemde beweging was niet gelijkmatig, waardoor de invloed van de draaiversnelling op de barbecue-reacties kon worden bestudeerd. De reactiepatronen op ieder der twee prikkels bleven voor een groot gedeelte onafhankelijk van elkaar bestaan, hetgeen aantoont dat de twee verschillende sub-organen, te weten de otolieten en de kanalen, verantwoordelijk zijn voor de twee reactiepatronen. Tevens toont deze proef aan dat het kanalensysteem in staat is otoliet-reacties te reguleren.

Eveneens hebben wij het effect bestudeerd van fentanyl en aethyl-alcohol op labyrinthreflexen, opgewekt door barbecue-rotatie. Fentanyl bleek de snelle fase van de nystagmus te onderdrukken, terwijl het perifere orgaan onbeinvloed bleef, zoals de langzame oogbewegingen aantoonden. Na alcoholtoediening aan het proefdier, kwamen wij tot de conclusie, dat positie alcohol nystagmus (p.a.n.) van centrale oorsprong en constant aanwezig is, doch gereguleerd wordt door de otolieten, afhankelijk van de orientatie ten opzichte van de richting van de zwaartekracht.

Wat wij zien na een unilaterale labyrinthectomie geeft ons de indruk, dat van twee intacte labyrinthen zeer dikwijls remmende invloeden op elkaar uitgaan.

De richting van de spontane nystagmus na een unilaterale labyrinthectomie verandert naar gelang van zwaartekrachtrichting indien wij het proefdier aan een barbecue-rotatie onderwerpen. Deze regulering van nystagmus kan worden toegeschreven aan de otolieten van de niet geopereerde zijde.

Ter verder onderzoek prikkelden wij de utriculus en de nervus utricularis mechanisch en elektrisch. In de geslaagde gevallen konden wij geen nystagmus opwekken door elektrische prikkeling van de utriculus noch van de nervus utricularis. Door middel van mechanische prikkeling van de macula der utriculus konden we inderdaad nystagmus opwekken, *terwijl hierbij een cupula beweging kan worden uitgesloten.*

Na een partiële labyrinthectomie beiderzijds waarbij de nervi utriculares werden doorgesneden, de sacculi verwoest en de kanalen intact gelaten, verdwenen de langzame oogbewegingen en de begeleidende nystagmus allebei. Dit bewijst dat zowel de langzame oogbeweging als de begeleidende nystagmus hun oorsprong vinden in de otolieten. (Het intact zijn van de kanalenfunctie werd bevestigd door de torsieschommeltest.) Ook bewijst het dat het kanalensysteem niet gevoelig is voor de werking van de zwaartekracht *en zeker niet kan worden beschouwd als een lineaire "accelerometer".*

De functie van de sacculus werd lange tijd niet als vestibulair beschouwd. Uit onze resultaten trekken wij de conclusie dat de sacculus wel degelijk een vestibulaire functie bezit. Het blijkt dat de functie van de sacculus normalerwijze door de utriculus wordt overschaduwd. Dit zou een van de redenen kunnen zijn die zovele auteurs in het verleden er toe hebben gebracht de sacculus als van niet-vestibulaire aard te beschouwen.

In dit werk stellen wij dat er tenminste twee verschillende reflex-bogen bestaan, te weten:

de cupula-oculaire en de otoliet-oculaire reflexen. Beide kunnen worden beschouwd als "feedback" systemen die met verschillende vormen van versnellingen te maken hebben, ofwel angulair of lineair. Zij werken min of meer onafhankelijk van elkaar ofschoon enig regulerend effect van de een op de ander (en vice versa) duidelijk kan worden aangetoond.

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STELLINGEN

I

De verfijning van de audio-vestibulaire onderzoekmethoden heeft de diagnostiek van brughoektumoren verschoven van neurologie naar keel-, neus- en oorheelkunde.

II

Het tonen van het verloop van een menselijke bevalling voor de openbare televisie moet op medisch-etische gronden ongewenst worden geacht.

III

Bij het vermoeden van een brughoektumor dient een cisternografie met lucht te worden verricht.

IV

De werkingswijze van de centra, welke de oogstand regelen, vertoont grote overeenkomst met die van een meervoudig vertakt regelnetwerk.

Holst, von E.
Naturwissenschaften 37-464-1950
Mittelstaedt, H.
Z. vergl. Physiol. 32-422-1950

V

Patienten met oorsuizingen dienen behalve door de K.N.O.-arts mede onderzocht te worden door de Mondheelkundige op mogelijke afwijkingen van kaakgewricht en gebit.

VI

Langdurige voortzetting van de behandeling met anticoagulantia, na het doormaken van een myocardinfarct, veroorzaakt een overtuigende, zij het bescheiden afneming in mortaliteit bij mannen onder 55 jaar. Boven deze leeftijd blijft het effect van deze therapie onduidelijk.

J.a.m.a. 193/1, 157, 1965

VII

Het verdient aanbeveling harttransplantaties te beoordelen naar hun wetenschappelijke achtergrond en niet op een emotionele basis.

VIII

Bij de behandeling van het cervixcarcinoom bestaat op grond van de 5 jaars overlevingsresultaten geen voorkeur voor radiotherapie boven operatieve behandeling.

Ann. report of treatment in
carcinoma of the uterus and
vagina. Vol, 14.