AGE AND VESTIBULAR FUNCTION

A nystagmographical study of vestibular tests in people of different ages

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Chapter I

INTRODUCTION

In a society consisting of individuals over a wide age spectrum, the age-related changes in the over-all functioning of these individuals may assume considerable importance. It is therefore necessary to assess the frequency with which major age-related changes occur. In the area of sensory functions, only vision and hearing have been studied extensively. Data derived from such studies give an indication of the distribution of impairment in the population, usually in terms of "bad vision" and "hard of hearing" conditions.

Age changes in vestibular function have received only scant attention in the literature.

The purpose of this thesis is to explore age changes in vestibular function by giving statistic results of caloric and rotatory tests performed on normal subjects of various ages.

GENERAL SURVEY

The growing interest in old people and in the process of ageing creates an increasing need of study concerning gerontology and geriatrics.

A discussion about ageing in general is followed by remarks about ageing processes in a few organs, where the neurological deviations can be summarized as "a reduction in neural excitability".

After a description of the embryology of the inner ear, with special attention to the development of the semicircular canals and pneumatisation of the mastoid part of the temporal bone, a detailed picture of the blood supply to the inner ear is given.

The review of literature continues with presbyacusis and more elaborately with presbyastasis, the latter expressing itself as a hyper-, or hyporeactivity, and the vestibular apparatus in children. A different pattern of reactivity is seen in new-borns, young children, and the older child.

Adaptation is discussed in connection with this changing pattern. The different pattern of reactivity from new-born to very old age, was studied in 8 groups of experiments, about thermic stimulation and rotational stimuli.

Chapter II

REVIEW OF LITERATURE

A. General aspects of ageing.

B. Embryology-anatomy of the inner ear.

C. Age and cochlea.

D. A detailed examination of the literature concerning ageing of the vestibular apparatus.

E. The vestibular apparatus in children, with a description of the changing physiology and function from new-born to adult.

A. General aspects of ageing

"Silver threads among the Gold" is only a very small aspect of ageing, the process of growing old.

Ageing starts after conception and the process continues throughout pregnancy, stages of birth, development, maturity, old age and death. The accent in our society is still on the old Greek ideal: youth, vigor and beauty, with the age group 18-30 as the ideal, but many intellectual young people are not mentally mature at that age. Vondel wrote his best drama's after the age of 63 years, Goethe's literary peak (Faust) was at 80 and Sophocles produced a drama at 90 years of age.

Clinical meaning of age

Age provides an indication of the various stages of development and the psycho-somatic functioning, the medical and physiological status of man at a certain moment, and is the product of:

1. his own inherent growth potential (Meyer 1970),
2. his ability to react against disease,
3. the number of times that certain illnesses knocked him over,
4. the cumulation of all previous traumata and diseases.

The chronological age is not a reliable standard for the functional age. Individual old people sometimes appear healthier than some average young ones. At most one can speak of a functional age per function, but not for a complex of physical, physiological, and psychological functions in total. These functions change, partly independantly of each other, and in a different tempo (Heron; Chown 1967). Those capacities that are used in daily life will retain a youthful standard longer. Tasks that call for a one-sided functioning, could lead to a decline in the capacity for other functions. This is called "the work feedback concept of ageing" (Smith and Greene 1962).

From a medical point of view ageing can be defined as:

1. a decrease of vitality
2. a progressive drop in biological efficiency
3. a blunting of the power of the organism to maintain itself as an efficient machine.

The tempo of ageing differs from organ to organ. Shock (1962) measured the physiological-anatomical decrease in organs from 30 until 75 years of age and found:

1.	brain weight	46%
2.	blood circulation to brain	20%
3.	resting heart output	30%
4.	plasma flow through kidney	50%
5.	amount of fibres in nerves	37%
6.	conduction speed of nerves	10%
7.	number of taste buds	64%

8.	maximum O_2-intake during exercise	60%
9.	vital capacity	44%
10.	strength of grip (hand)	45%
11.	body water contents	18%
12.	body weight (man)	12%

The clinical problem in medicine is to distinguish between a decline in vitality as a result of ageing, and from a decline in vitality as a result of trauma and disease.

Anatomical and histological changes in organs as a result of ageing

Brain and nervous system

In man, changes in brain function are dominant, and we see symptoms and signs of deterioration in functioning of the brain, such as a decay of personality, the trembling of hands, a softer voice, obstinacy, and depressive moods. Maniac depressive psychoses, as a result of brain involution are a very common psychiatric condition during this phase of life. Most workers describe changes in Nissl material and nuclei of neurons and also a true degeneration of neurons, with an increase of neuroglia cells. According to Critchley (1956) the most constant neurological deviations in old people are:

1. presbyopia
2. presbyacusis
3. retarded activity
4. retarded reaction time
5. decrease in speed of perception
6. defective conjugate upward gaze
7. shortening of convergence reflexes
8. bent posture
9. decrease in vibration sense
10. loss of fine co-ordination
11. decrease in muscle power and atrophy of muscles.

These points can be summarized as "a reduction in neural excitability, one manifestation of which is a loss of central inhibitory control" (Birren 1947, 1959).

Muscular system

A decrease in the total amount of muscle fibres runs parallel with the reduction in brain weight.

Skin and supporting tissues

Changes with ageing here are very prominent e.g.: fine wrinkles, loose skin, prominent temporal vessels, greying, and loss of hair.

Cardio-vascular system

It is difficult to distinguish between changes due to ageing and changes due to pathology, especially concerning atherosclerosis and hypertension. It is still an unanswered question whether atherosclerosis is a pathological process or a factor of ageing. Two mechanisms prepare the road for atherosclerosis: changes in blood chemistry and age-changes in vessel-walls.

Skeleton

Osteoporosis is seen mostly in older people, more often in women than in men (Gitman 1965).

Nose

The droop of the nasal tip in advanced age is due to changes of the shape and of the structure of the lobular cartilage. In young people this cartilage is convex and rather resistant. In advanced age it is straightened and segmented so that it becomes larger in cranio-caudal direction and shifts caudally (Krmpotić-Nemanić, Kostović, Rudan and Nemanić 1971).

Theories about ageing.

1. Wear and tear theory (Rubner 1908): life span runs parallel with metabolism. Metabolism of rats increases in cold weather, and so their life span is shortened (Johnson 1961).

2. Stress theory (Selye 1956). In rats different types of stress show changes corresponding with ageing. Others see disease as primary a stress factor (Jones 1956).

3. Collagen theory. Ageing is accompanied by changes in the collagen of the body. Stress causes the formation of depot-collagen.

4. Waste product theory: Certain waste products of metabolism are inefficiently excreted and cells are intoxicated and die. These products, however, have never been found. Strehler (1959, 1962) suggests lipofuscine to be the causing agent.

5. Mutation theory: Spontaneous mutation is found in the cells of the body. This process changes cell function, and cells may eventually die. X-rays give cause to cell mutation which promotes ageing.

6. Auto-immune theory. Auto-immune diseases such as arthritis, muscle dysthrophy, and diabetes mellitus are very prominent. If the immunological character of a cell changes (mutation), this cell behaves like a foreign cell and is rejected.

7. Combination theory. A frame for different conceptions (Burch 1963; Curtis 1966; Meyer 1970).

B. Embryology-Anatomy of the inner ear
(Anson, Harper, and Winch 1966).

I. The structure of the vestibular apparatus is far less complicated than that of the organ of Corti and there is also an important phylogenetic difference in that the semi-circular canals, utriculus, and sacculus are already present in selachian fish. The cochlear part of the stato-acoustic organ, which is much more "sophisticated" in man, undergoes a dramatic conversion, whilst the vestibular part retains much of its earlier simple status. It is generally accepted that these primitive organs have a better resistance against ageing than the more highly differentiated tissues of the organ of Corti.

II. *The inner ear* (Cunnigham, Bok, Altmann, Beck).

The inner ear consists of the bony labyrinth in the petrous part of the temporal bone, and the membranous labyrinth contained within.

a. *The membranous labyrinth* (endolymphatic system). The formation of the membranous labyrinth in the human being starts at a very early stage with a thickening of the surface epithelium of the neural plate during the first week of embryonic life. This thickening, the ear placode, is growing into a pit formation and with 21 days is called the ear-pit. The ear-pit deepens, closes dorsally and thus forms the ear-vesicle which looses its contact with the surface epithelium at 29 days of embryonic life. On the 31st day the dorsal part of the vesicle changes its shape, which results in the very early recessus labyrinthi which will later form the ductus and saccus endolymphaticus. The place of origin of the recessus is marked by a fold coming from the dorsal wall and projecting into the lumen of the vesicle. This fold is called Fold I of Bast, Anson, and Gardner. Together with the formation of the recessus labyrinthi the ear-vesicle undergoes a subdivision which eventually results in several communicating cavities. During the 5th week of intra-uterine life the vesicle divides into a bigger (dorsal) and a smaller (ventral) part. The semicircular canals develop from the dorsal part, first the two vertical ones, then the horizontal canal. The canals are well developed in the five weeks old embryo. The semicircular canals grow during the first half of the embryo's intra-uterine life and reach their ultimate size during the twentysecond week. The rest of the dorsal part is called vestibule.
Shortly after the semicircular canals start to develop, the ventral part of the vesicle elongates, takes a curved shape and is called the duct of the cochlea. On the place where the duct of the cochlea descends from the vestibule the ductus re-uniens originates. It is fully developed at eight weeks. During the seventh week of fetal life the subdivision of the vestibule into utriculus and sacculus starts by means of the outgrowing of a fold from the lateral wall of the vesicle to the inner opening of the

endolympathic duct of a similar fold from the medial wall of the vesicle. This latter fold is called Fold II of Bast, Anson, and Gardner, the former one the Fold III of Bast, Anson, and Gardner. The three folds grow out and result in the final anatomical relations between utriculus and sacculus and endolymphatic duct which are laid down round about the tenth week of embryonic life. Fold I is then called utriculo endolymphatic valve of Bast. This valve will take care that, when endolymphe is withdrawn from the sacculus, the utriculus will keep its expanded form, but not the other way round. The endolymphatic duct is the only part of the membranous labyrinth that continues growing until in the adult stage.
The histo-morphological appearances in the immediate surroundings of the developing endolymphatic system are the following: In the very early development the mesenchym immediately around the ear-vesicle (otocyst) thickens and differentiates during the seventh week of intra-uterine life into precartilage. The outer layer changes into cartilage and the inner layer into reticulum with mesh formation. These meshes get bigger and bigger and disappear at some places. In this way the perilymphatic system develops. By bony changes in the surrounding cartilage the pars petrosa of the temporal bone is formed.

b. This *bone formation in the cartilaginous labyrinth* surrounding the membranous labyrinth starts during the fourth embryonal month and is completed at birth, so the bony labyrinth has got its ultimate shape and size in the new-born baby. This final shape is little affected by general growing-influences on other bone structures (Beck). The bony labyrinth has got the hardest body (Sato 1903; Siebenmann 1890). It is divided into three parts:

1. a small chamber, called the vestibule
2. a coiled tube the cochlea, in front of the vestibule
3. three semicircular canals behind the vestibule.

The cochlea and the canals communicate freely with the vestibule. All parts have a delicate lining of endosteum.
The bony labyrinth consists of three layers, the outer or periostal layer, the middle or enchondral layer which is considered as embryonal tissue — this is the only place in the human body where it is preserved into the highest age —, and the inner or endostal layer.
These three layers can always be seen very clearly in the cochlea, but are not so distinct in the vestibulae and semicircular canals.
For instance in the superior canal the enchondral layer may be missing. Increasing age does not cause any changes in the endostal layer but in the enchondral layer a narrowing of the blood vessels is sometimes found because of increasing sclerosis. With increasing age bone destruction in the periostal layer becomes apparent, causing the formation of narrow spaces.

c. *Development of semicircular canals after birth*

Sato (1903) measured and compared the development of semicircular canals in the labyrinth of fetus, neonatus, and adult. Meckel (1827) thought that the form and dimensions of the canals change remarkably after birth. Hyrtl (1845) found an increase in length and width of the canals with increasing age. Siebenmann (1890) measured the angles which the planes through the canals form with each other. Sato (1903) stated that individual differences may exist in the shape and dimensions of the semicircular canals but that the left and right canals show a marked similarity in the same individual. Most authors are in agreement on the circumferential lengths of the three canals and claim that the posterior canal is the longest, the horizontal (lateral) the shortest, and that the increase in length from fetal size to adult size is greater in the posterior canal and less in the superior one. The size of the lumen of the posterior canal is the greater and that of the superior canal the smaller in all age groups. The diameter of the canal is usually increased at the ampulla, except in the case of the posterior one. The diameters of the canals are not increased in adults, but are usually smaller than in new-borns. The ampullae too do not increase in size with age after birth. *Angle of inclination of the canals:* this angle is somewhat smaller than 90° between superior and lateral semi-circular canal, is 90° for superior and posterior canal, but greater than 90° for posterior and lateral canal. Only the angle between posterior and lateral canal shows an increase with age. The lateral canal takes most part in the outward growth of the skull. We do not know the physiological meaning of this growing out of the horizontal canal.

d. *Pneumatization*

In the temporal bone, above all in the mastoid part, pneumatic cells are found. The process of pneumatization originates in the tympanic cavity and starts after birth. It is completed at the age of five years, but continues very much more slowly into high age (Beck 1963). The extension of the pneumatization may vary remarkably and between the picture of hundreds of little spaces separated by thin walls, and of no cells at all (in 19.5% of mastoid parts, Müller 1960), are lots of transitional stages. The size of the mastoid part of the temporal bone is influenced by the pneumatisation process, and a well pneumatized mastoid is approximately 1.5 cm bigger than a compact one.
There are also air-cells seen in the zygomatic process of the temporal bone and perilabyrinthal. The perilabyrinthal cells can extend into the pyramid, and pneumatisation of the pyramid-top is seen in 24-35% of people (Kraus 1931; Belinoff, Balan 1930). This depends on the degree of pneumatization of the mastoid part (Mellinger 1939). The pneumatization of the temporal bone is influenced by:

1. *Hereditary factors.* There exists a certain predisposition to more or less pneumatization, constitution also plays a role (Albrecht 1924, 1936; Schwarz 1958; Witmaack 1932; Diamant 1940, 1941, 1957, 1958, 1962; Müller 1960; Oltersdorf 1953, 1962).

2. *External factors*, like otitis media in infants and young children, causing damage to the mucosa, and inhibition of the pneumatisation process (Witmaack, 1918). Tumarkin (1957) states that the external influences can work until well into puberty.
It is important for the development of a well pneumatized mastoid process that the Eustachian tube functions normally (Krainz 1924; Link, Handl 1954; Oltersdorf 1962).
Todays opinion is (Beck 1963) that the process of pneumatisation is primarily an expression of heredity. Between a well pneumatized and a not pneumatized mastoid part of the temporal bone are fluctuations that can be brought back to developmental powers (Schwarz 1958). Environmental factors are of subordinate importance.

III. *Blood supply to the inner ear*

The blood circulation through the labyrinth is of primary importance for its function. The basilar artery plays the major part (Fields 1964). It is a midline trunk and receives its principal blood supply from the confluence of the two vertebral arteries. The basilar artery can also receive blood from the carotid system on either side, through the posterior communicating arteries of the circle of Willis. Anomalies in arterial development occur with a high degree of frequency in this part of the cranio-cervical circulation. The circle of Willis, extremely important as potential source of anastomotic flow in the arteries at the base of the brain, is frequently defective in one or more of its segments. The most common variation observed is the persistence of a primitive embryologic pattern in which the posterior cerebral artery on one or both sides originates from the internal carotid arteries, without any, or only a tenuous communication with the basilar artery. As a consequence of these variations, the potential for collateral blood flow under pathological conditions is greatly diminished.
The arterial blood supply of the labyrinth comes from the Art. labyrinthi (Art. auditiva interna), which originates from the basilar artery, comes through the meatus acusticus internus and usually divides into three main branches (Siebenmann 1894).

a. *Art. Vestibularis*

The Art. vestibularis supplies the semi-circular canals, the ampullae, and the posterior parts of utriculus and sacculus.

b. *Art. Cochlearis*

The Art. cochlearis by dividing into three branches, supplies the cochlea except for a part of the basal coil.

c. *Art. Vestibulo-cochlearis*

The Art. vestibulo-cochlearis supplies with the ramus cochlearis the basal turn of the cochlea and forms here a large anastomosis with the Art. cochlearis. With its ramus vestibularis it supplies the lower half of the semicircular canals and ampullae, with a separate branch to the macula sacculi.

C. Age and cochlea

Presbyacusis is the term that describes the effect of ageing on hearing and refers to changes in the cell structure. This is primarily a degenerative process, but is considered to be physiological, like presbyopia and other bodily changes related to ageing.

These changes occur independent of environmental influences (Glorig and Nixon 1962). It is difficult to differentiate between changes caused by injuries and diseases, and the normal changes of ageing. Zwaardemaker (1894) described atrophic changes in the basal turn of the cochlea as the underlying pathology. Mayer (1920) stated that the ageing process in the cochlea is due to increasing rigidity of the basilar membrane. Saxen (1937) described an atrophy of the spiral ganglion and severe changes in the cochlear duct, causing flattening of the strial epithelium, hyalinization of blood vessels in the stria vascularis, collaps of the organ of Corti, and adhesions of Reissner's membrane to the strial epithelium. These changes are equally marked in all parts of the cochlea, and are caused by capillary sclerosis in the stria vascularis. Schuknecht (1955, 1964) described degeneration of the organ of Corti with loss of the hair cells and supporting cells. This atrophy was most severe in the basal part of the cochlea. Fleischer (1956) detected as only change the loss of ganglion cells in the basal part of the cochlea, demonstrable from the 3rd to 4th decade. Van Dishoeck (1966) described a histopathological picture of presbyacusis, limited to a part of the cochlea. There is loss of ganglion cells in the basal turn of the spiral ganglion, the part of the cochlea where high tones are perceived. With advanced age a degeneration of the central hearing pathways and hearing centres also occurs. The organ of Corti shows degenerative changes as a result of angio-sclerosis. Another important cause of a high-perception loss is noise, and here too the basal turn of the cochlea is selectively attacked. Rosen et al. (1962) tested Sudan blacks, who live in practically noisefree surroundings. He found no presbyacusis in these people, and even at advanced age their hearing was equal to that of Europeans of 30 years of age. He concluded that ageing of the hearing organ may be influenced by a great variety of factors, both physical and environmental. The following lesions, alone or combined, have been named as possible causes of presbyacusis:

a. atrophy of the spiral ganglion and associated nerve fibres

b. angiosclerotic degeneration of the inner ear
c. loss of elasticity of the basilar membrane
d. causes, originating in the central nervous system
e. apposition of bone at the base of the internal auditory canal resulting in closure of the canaliculi at the origin of the foraminous spiral tract (Krmpotić-Nemanić 1963, 1969).

Senile atrophy of the spiral ganglion becomes more pronounced with advancing age, and occurs independently of local arteriosclerosis. It seems that ganglion cell atrophy and degeneration of the hair-cells (of Corti's organ) are two different entities, and are not caused exclusively by ageing. Most authors (Beyermann-Gröszer 1954 and Matzker 1954) assume a contributory central cause for presbyacusis, but so far no experimental proof for this view has been provided. According to Matzker (1954), poor hearing found with binaural testing is conclusive for a central lesion. After the 4th decade of life, he found a pronounced decrease in central synthesis of two binaurally applied acoustic halves. Sércer and Krmpotić (1958) found a progressive apposition of bone at the fundus of the internal auditory canal, beginning rather early in life and similar to the apposition of bone in the ageing skull. They found the same phenomenon in the lamina cribrosa, leading to loss of smell. This condition causes a compression-closure of the canaliculi and results in atrophy of the nerve fibres and spiral-ganglion cells. All investigators agree that the pathological changes are more pronounced in the basal turn of the cochlea, the corresponding ganglion cells, and the nerve fibres. The role of noise in presbyacusis should not be overevaluated, since with ageing various metabolic changes as well as physical changes take place in all tissues, particularly the connective tissue. Such changes may affect all the structures of the inner ear. Atherosclerotic changes are continuing simultaneously, and these also could affect the circulation of the inner ear.

D. Age and vestibular apparatus

The decline in visual and auditory performance with advancing age is well known. Taste and sense of smell also show regression (Zilstorff-Pedersen and Feldman 1962). It stands to reason therefore that the performance of the vestibular organ also deteriorates with increasing age and it has been established that there is a decrease in the number of fibres of the vestibular nerve, that the sensory cells atrophy, and that the semi-circular-canal walls show osteoporosis (Haas 1964).

The compensations of the vestibular damages are much greater than those of the acoustic part (Ferreri 1954; De Vido and Pagnini 1956). The absence of clinical manifestations of the aged vestibular apparatus is one of the reasons why no specific interest has been taken by researchers in the consequences of its senile degeneration.

The posterior labyrinth is well preserved throughout the advancing years (Ferreri 1954) and only very rarely, although a diminuation of hearing occurs, do old people show vestibular symptoms. Vestibular disorientation in old people is more often the result of uncertainty and blurring of vision than of true vertigo. Droller and Pemberton (1953) found vertiginous disturbances in 47% of men over the age of 67 years and in 61% of women over 62 years of age. This was attributed to arteriosclerotic lesions in the vestibular receptors. Other authors noted a certain frequency of vertiginous attacks in elderly people. Aubry (1955) described a slight vertigo, often accompanied by an unpleasant tinnitus in some senile patients. Vestibular signs in these cases were very rare, and at the most a slight degree of vestibular hyporeflexia was present.

Comel (1932) examined vestibular function (caloric test, Kobrak technique) of a group of patients over 70 years of age and saw a certain relation between the anatomical condition of their nose and the function of the cochlea-vestibular apparatus. There was an increase of vestibular reflexes on the side where a nasal obstruction existed, as a result of a deviation of the nasal septum. Scuderi (1947) found an increase in vestibular reflexes of a group of old people, normal reflexes in others and a diminuation of reflexes in a third group. He also found different results on different occasions in the same people and considered this to be due to the blood circulation at the times of examination. It is obvious that the blood circulation of the inner ear in elderly subjects is not normal, and depends on the degree of atherosclerosis. Pallestrini (1933) divided atherosclerosis of the labyrinth into two stages, i.e. angio-neurosis ("vasospasm"), followed by angio-sclerosis. He found, as did Scuderi (1947), that most cases belonging to the angio-neurotic stage presented an increase in vestibular reflexes, whilst a decrease was found in the angio-sclerotic stage.

Zelenka and Kozak (1963) examined 132 patients with varying stages of hypertension and sclerotic disease, ranging from vaso-spasm ("angio-neurosis") to frank atherosclerosis. All tended to show postrotatory hyper-reactivity. The vestibular neurons which suffer earliest from the ischemia of age and disease appear to be those mediating inhibitory activities. Arslan (1957) examined 50 people between 49 and 84 years of age (caloric stimulation, Veit's technique) and found 30 cases with decreased, 6 with increased, and 14 with normal caloric reflexes. His middle-aged subjects appeared hyper-reactive and the subjects over 70 hypo-excitable. The reflex-action was usually better on the side with the better hearing and there proved to be an inconsistent relationship between hypoacusis and vestibular reflex-action. He explained the hyperreflexia after thermic stimulation in subjects affected by atherosclerosis to a larger or lesser degree as a decrease of the inhibition normally exercised by the supra-nuclear structures (cortical, cerebellar,

and mesencephalic). Camarda (1956) using angular rotation in a group of old people found that under the same circumstances vestibular stimuli give less vegetative reactions than in a young group. This is easily explained since the sensation of rotation is a perceptive phenomenon and old people show a delay in recording their nervous and perceptive sensations. Rossberg (1964) studied post-rotatory nystagmus in a group of people from 20 to 80 years of age and found a reduction of the excitability of the vestibular system with advancing age.

Meyer zum Gottesberge (1950) and Maurer (1950) found a reduction of the vestibular regulatory function in elderly people, and thought it to be caused by a depression of the vestibular centres (where co-ordination takes place). He concluded that there is a reduction of peripheral vestibular excitability with increasing age, as well as a reduction in the regulation of vestibular co-ordination.

Bony changes

Krmpotić and Nemanić (1969) discussed diminished hearing ability in old age, the reduction of vestibular and olfactory functions and considered it to be caused by analogous biological processes. The conception of progressive senile anosmia is based on histological changes described by Prevost (1958). Only a few authors (Portmann et al. 1960, Hofmann 1926, Vaschide 1905), however, mention it. The reason why changes in the cochlear apparatus have been investigated and discussed more often than those of the vestibular and olfactory apparatus, lies in the fact that the changes in hearing become manifest more early than those of the vestibular and olfactory sense organs. The vestibular apparatus has a greater possibility of being compensated; whilst slight changes in the olfactory apparatus cannot easily be recognised so that they remain hidden for a long time. The cochlear nerve, vestibular nerve, and fila olfactoria are sensory nerves and conduct stimulations from the corresponding sensory organs. These three nerves on their way from the sensory epithelium to the central nervous system pass through a system of tiny holes in a thin bony plate. In these tiny holes a piling up of a bony substance takes place from the fetal period until the end of life. Krmpotić (1969) found, on examining one hundred skulls, that the number of holes in the spiral tract (tractus spiralis foraminosus) as well as in the vestibular area (of the internal auditory canal) is progressively reduced with advancing age. The reduction in the number of holes was greater in the basal turn than in the modiolus region. On cross-section through the spiral tract it was established that the endostal bone which forms the tractus, increases in thickness by ten from the fetal to the adult period of life. Analogous thickening of the bony substance, and reduction of the number of openings in the vestibular, saccular and utriculo-ampullar area were more obvious when present, because the number of holes being fewer from the beginning

could be more easily counted. This piling up of the bony substance develops progressively. At the end of the 6th or beginning of the 7th fetal month, the openings in the spiral tract are large. By the apposition of bony substance in the region of the tractus, the holes become smaller and the bony substance between them thicker. In the fetus the number of holes varies from 100 to 140 diminishing in adults by a third. Krmpotić described bony cuffs surrounding the artery in 13 specimens (64-78 years) in the region of the entrance of the cochlear branch of the Art. auditiva interna. According to Schwartze the branches of the Art. auditiva interna enter the cochlea through the central canal, through one of the openings in the spiral tract. The cuffs were found in these cases at the beginning of the basal coil only. Histological sections were made through the acoustic nerve, near the fundus of the internal auditory canal, in order to demonstrate the consequences of these changes on the nerve fibres in the fundus. The nerve in the region of the fundus is divided into small bundles and has a sheath of connective tissue up to a length of 2 mm. From that point centrally Krmpotić found glial elements in the nerve. In cadavers of elderly people the nerve was cut very close to the fundus in the region where the number of holes in the tract is reduced, and it was found that the number of fibres in this area was also reduced. The number of nerve fibres in the acoustic and vestibular nerve was not counted systematically, but from the number counted, the findings of Rasmussen (1940) could be substantiated. According to Rasmussen the number of cochlear fibres is reduced with age by more than half, but the vestibular fibres to a far lesser extent. The absolute number of cochlear fibres is bigger than that of the vestibular fibres. The reduction with increasing age of fibres is in general symmetrical and so is the reduction of the number of openings in the spiral tract. Unfortunately no audiograms of the examined cases were available. An analogous process was found in a third region where nerve fibres run through a system of tiny holes, the area of the lamina cribrosa of the ethmoid. In this area the number of holes is reduced in the postero-anterior direction by thickening of the lamina cribrosa (first described by Knajfel). Cases were found with a complete disappearance of holes and nerve fibres in the posterior region of the cribrous plate. In this case it was easier to prove that a reduction in the number of holes took place, because the cribrous plate is more accessible than the fundus, and the number of holes smaller than in the spiral tract. All three processes described in senescene are the results of the deposits of bony substance in the region of nerve-openings. This causes narrowing of the holes with the formation of tiny bony canals which, in turn, are eventually obliterated. This process leads to compression of the nerve fibres followed by atrophy and loss of function. In analogy with presbyacusis the changes of the vestibular and olfactory functions due to ageing are called presbyastasis and presbyosmia. Naumann (1968) tested different age groups in connection with the olfactory sense, and found a decline with increasing age. Krmpotić (1969) proposes that the apposition of bone comes first, followed by the degeneration of the nerve, and that the vascular element is of less importance than the bony changes.

Vascular changes

The vestibular mechanism is very sensitive to local changes in arterial circulation but is also easily affected by circulatory changes of a more remote origin.

Lowered blood supply through the basilar artery leads to ischemia of brain-stem structures. This condition causes a syndrome which includes equilibratory, visual, auditory, as well as somatic motor and sensory disturbances. Vertigo is the most common symptom (Denny-Brown 1949, 1952, 1953; Millekan and Siekert 1955; Sillevis Smitt 1959; Fields 1964). The latter author did 2000 bilateral angiographies to screen the entire arteriolar tree, to ascertain whether occlusive lesions were present in the cervical and cranial arteries, and to determine the quality of the collateral circulation. Most disturbances of basilar vertebralis circulation are seen in elderly people. This fact gives a strong indication that atherosclerosis, like mechanical compression in cervical arthrosis (Brain 1963), is a causative factor. The symptom in these cases is postural dizziness. Other clinical findings are high blood-sugar values, sometimes heartfailure but, surprisingly, no hypertension (Orma and Koskenoja 1957). As a result of atherosclerosis the labyrinth is subject to degeneration. Williams (1963) found degenerative changes in the macula and cristae with advancing years caused partly by inadequate nutrition. The entire condition cannot be explained on this basis. An important part of these degenerative changes can only be termed as "*the process of ageing*".

Patenostre (1912) uses the term "senile mastoid", and distinguishes (according to the thesis of Depoutre (1912)) two types: the ivory type (rarely seen) and the pneumatic type (frequently seen). He compared the results of audiometric and caloric tests, and concluded that the vestibular part of the labyrinth shows a decrease in reactions to these tests in elderly people (60 to 70 year age-group) when compared to the results from a younger group. Similar findings were obtained in the cochlear part, but to a more severe degree. Zelenka and Slaninova (1964) came to the same conclusions, i.e. that senile changes have their effect on the entire labyrinth. The predominance of auditory symptoms is due to the greater sensitivity of the cochlear part of the labyrinth to harmful agents like noise, trauma, and some antibiotics. The vestibular apparatus seems to be much more resistant to senile changes, and spontaneous symptoms are only rarely found. From their experiments it is apparent that at about 20 years of age the reactivity of the

vestibular apparatus begins to increase with age, attaining maximal reactivity in the fourties and fifties. After the age of 60, responsivity tends to decline, and the authors called this senile *hypo-reactivity*. The authors further propose that hyporeflexia in children is due to a still imperfect connection between the vestibular and oculomotor pathways. Normal functioning is only possible after linkage of both pathways is accomplished. This process is enhanced by personal experience and individual training at different ages.The reflexes then become normal. Malkevick (1963) tested 97 people of 50 to 90 years of age by means of rotation and calorization, and observed changes that were of central-nervous origin. The findings generally conformed with an increased inhibitory influence of the cortical part of the central nervous system which controls the labyrinth. Haas (1964) tested 104-subjects aged 15 to 80 years, with Montandon's method of determining the rotatory threshold and concluded that the organ of balance showed a diminishing function with increasing age. Chladeck (1966) took cupulograms of 51 subjects aged 60 to 75 years (27 with pure presbyacusis, 24 with a more severe defect of hearing) and obtained normal results in the group with presbyacusis and for the other group the supra threshold post-rotational excitability was frequently raised. So they revealed a post-rotational hyper- reactivity, but the caloric reaction was reduced in all cases. With regard to response changes following repeated caloric tests in relation to age, Gramowski and Unger (1969) noticed a more prominent decline in response in 60-70 year-old subjects than in 15-25 year-olds receiving five cold irrigations at eight-minutes intervals. All subjects in this study showed some response decline upon repeated testing. The authors, however, expected a greater decline in reactions in young persons, because they supposed that this decrease in reaction to repeated stimuli was the result of training (process of learning) which, according to them, should be better in young people. They now tried to explain the greater decline in response in the older group as follows:

firstly, older people are more quickly tired than young ones, when repeated stimuli are given (fatigue),

secondly, old people could have a deficient natural habituation or a complete loss of natural habituation.

This natural habituation develops and grows in young people, where stimuli from every-day life, such as sport, dancing, cycling, and skating, build up a changed vestibular status. This natural habituation we will call in future "Habituation".

Before continuing with the decrease in vestibular reactions with ageing, we want to discuss "**Fatigue, Habituation, and Adaptation**".

Fatigue stands on its own when we discuss a decrease in reaction after a certain stimulus — mostly repeated stimuli — and depends on various factors like time of the day or night, the amount of given stimuli, the constitution and nutritional status of the test-person, and his age. It is

well-known that older people are more quickly tired than young ones, when repeated stimuli are given.

Habituation and *adaptation* are not always clearly separated in literature. Whereas adaptation means a decrease in reaction during one stimulus, habituation is the decrease of the reaction after repeated stimuli.

The ability not to react on biological meaningless stimuli is a very important phenomenon, which, for vestibular reactions, was already recognised many years ago (Abels 1906). Habituation is a process of learning, with the typical characteristics: acquisition (the learning phase), the phase of transfer (of this habituation) to certain other vestibular stimuli, and the phase of storage, i.e. retention ("keep it in mind") for a certain time after the phase of learning. Vestibular habituation of course is an important part of the insensitivity to motion-sickness, and therefore important to seamen (De Wit 1953), pilots (Krijger 1954; Aschan 1959), figure skaters (McCabe 1960; Collins 1966), and ballet dancers (Dix and Hood 1968).

The second world war strengthened the interest in habituation (troop-ship transports) and most contributions in this field come from the U.S.A. During the last years this interest has been intensified on account of the space-programs.

With habituation — as said before — we mean the natural habituation i.e. the changing of the vestibular status as the person grows, develops, and learns; the ability to adapt himself to new different, sometimes whirling situations. There should be a peak performance of this phenomenon during the physical active periods of life, when profession or sport demands a lot of the sense of equilibrium. The bigger loss of reaction rates in older subjects originates from a reduction or loss of natural habituation. A decrease of central inhibition would seem the likely neural correlate of this process.

With experimental habituation is meant that a *temporary* habituation develops as a result of a series of artificial vestibular stimuli. It is a "getting used" to proceedings in the vestibular apparatus, and is also called, though incorrectly, adaptation: the vestibular apparatus adapts itself to this one and only series of stimuli.

Minnigerode and Grohman (1966) tried to find standard characteristics in the electronystagmograms with rotatory acceleration stimuli of healthy test subjects of different ages (0-65). They found that the total amplitude (the sum-total of all individual amplitudes of the recorded nystagmus beats during a nystagmus period) decreases with increasing age, and considered the amplitude in all periods of the nystagmus duration to be a quantitative parameter and a good standard for the intensity of a limited nystagmus event. They claim a systematic response diminuation with age. This was also found by Dohlman (1935); Jung and Tönnies (1948), and Mittermaier (1954).

Caloric tests were performed on 293 screened dizziness patients (Bruner and Norris 1971) ranging in age from 20 to 88, and the caloric nystagmus was studied. All nystagmus parameters revealed increased responsitivity with age into the 60's followed by a decline in the over 60 age-group.This was shown best by frequency and slow-phase velocity and to a smaller extent by amplitude, latency, duration, and fast-phase velocity. Age increments in nystagmus were more pronounced for warm stimuli than cold. The incidence of spontaneous or positional nystagmus did not vary with age. The author offered a speculative explanation of the observed age effects that was based on vascular influences and loss of central inhibition. The most important finding here was: Hyperactivity until in advanced middle age, followed by a hyporeactivity for the older groups. This is also stated by Camarda and Lumia (1959). They used rotational stimuli in 23 subjects aged 70—92, and found higher thresholds than those considered normal for young adults, and a loss of vestibular excitability in old people. Okano (1938), like most authors, found after testing a group of people ranging in age from 60—80, a vestibular response decrement after the 7th decade.

Brookler and Pulec (1970) reported that the distribution according to age of the patient (they used the records of 4950 E.N.T. patients between 15 and 74 years of age) revealed that responses to warm water (44° C) showed no change with increasing age but responses to cold water (30° C) showed a small but clear decrease with increasing patient's age. *"Hyperreactivity"* of the vestibular system is described by Kotyza (1939). This author studied 117 healthy subjects between 11 and 63 years of age using caloric and rotational stimuli and concluded that the labyrinth is most responsive in the 5th decade.

Guedry (1950) studied two small groups (19—21 and 30—53) and found heightened vestibular effects for the older subjects. He thought that "older subjects may have less central control over the vestibular reflex system".

Chladeck (1966), as mentioned before, found some post-rotational hyperreactivity in people between 60 and 70 years old. Gramowski and Unger (1969) found, as stated before, in old people some heightened initial response levels, but as a whole, there was a diminuation of reactivity.

The reports found in literature about "*no change at all* with increasing age" are very few. Bourlière (1948) tested 160 women from 20—84 years using galvanic stimulation in order to elicit head movements and concluded that vestibular excitability is not affected by age. Further inspection of Bourlière's data (Weisz 1959) revealed that the vestibular excitability was slightly higher in the 5th and 6th decades than in the 4th, suggesting a two-phased ageing function with a responsivity peak in middle age.

Forgacs (1957) tested 80 nursing-home residents over 55 years of age,

with both rotational and caloric threshold tests, and reported "normal" vestibular reaction in all cases. Fregly and Graybiel (1970) administered threshold caloric tests to 76 vertiginous patients of 20—72 years old and reported that caloric thresholds were independent of age, although no specific analysis was described.

To summarize the situation we can say that the principal ageing effects reported in the literature fall into 3 classifications:

1. Hyporeactivity
2. Hyperreactivity
3. No change with age.

Group I. These authors mostly described a peak responsivity in middle age, followed by a *hyporeactivity* in senility. (Arslan; Aubrey; Brooke and Pulec; Bruner and Norris; Camarda and Lumia; Camarda and Tarsitano; Chladeck; Gramowski and Unger; Haas; Malkevich; Meyer zum Gottesberge and Maurer; Minnigerode and Grohman; Okano; Patenostre; Rossberg; Scuderi; Zelenka; and Slaninova).

Group II. *Hyperreactivity* is mentioned by Comel, Guedry, Gramowski and Unger, and Kotyza.

Group III. *No change* is reported by Bourlière; Forgacs; Fregly and Graybiel.

E. Children and the vestibular apparatus

At the two poles of life, infancy and old age, there are great differences in structure and function. These differences give reason to speak of the anatomy and physiology of infancy and the anatomy and physiology of old age (Galebsky 1924). From the embryology it is learned that the semicircular canals are formed during the 5th or 6th week of embryonic life; first the anterior and posterior canals, followed by the lateral canals after a short time. The parts of the labyrinth which control the equilibrium functions are ready to operate at this stage. The vestibular apparatus of the fetus and newborn is completely developed and differs only from the vestibular apparatus of adults in size and situation (see before, Embryology-Anatomy). Galebsky found:

1. All 3 semicircular canals react immediately after birth to rotation and calorization giving the appropriate type of nystagmus.
2. The reaction of the new-born *during* rotation differs from rotatory reaction in adults; a. in its intensity; b. in strongly pronounced movements of the head in the direction of the slow component of the nystagmus; c. in the absence or very weak character of the quick component.

Bárány stated in 1918 that the slow component of the nystagmus originates from the vestibular nuclei, whereas the quick component is the result of cerebral function (see later, origin of quick component of nystagmus). Bartels (1910) mentioned the absence of the quick com-

ponent in underdeveloped children where the brain is not yet fully developed.
De Kleyn (1911), however, states from his investigation of an anencaphalic monstrum that the quick component can only originate in the region of the vestibular nuclei. Galebsky (1924) states that the quick component does not originate in the brain, but in the region of the vestibular nuclei (for more about the origin of the quick component, see later). In new-born infants the cerebrum is still underdeveloped and incompletely myelinized (Vogt 1905). From the fact that the vestibular apparatus is well developed early in intra-uterine life, and all components functioning in the first extra-uterine hours (perhaps even during intra-uterine life when it seems of no use whatsoever) Galebsky (1924) took the liberty to conclude that "the function of the vestibular apparatus in the new-born infant, and may be also in the fetus, forms a repetition of a very old stage in the evolution of the nervous system, which in its time was of great importance".
This hypothesis is supported by the belief that the centres where nystagmus is elicited in the new-born are embedded in the palencephalon. The palencephalon is the oldest portion of the brain that already exists in fishes; and here the semicircular canals are well developed. During intra-uterine life the fetus can be compared with a fish. It swims like a fish in the uterine fluid and uses the highly developed vestibular apparatus for positioning itself in different positions. The obstetricians may therefore be wrong when they use the mass of the child's head to explain the changes in the unborn child's position within the uterus. The vestibular apparatus plays an important part in this respect.
Bartels (1910) was the first to examine the reaction of the vestibular apparatus in neonati by means of rotation. He noticed a nystagmus during and after rotation and found the strongest reaction on the seventh day after birth. He noted further that if the head was suddenly flexed, the upper eye lid was lifted and the forehead puckered via a vestibular reflex. This phenomenon was later confirmed by Bárány who also agreed with the statements of Bartels and Alexander (1911) that the head movements evoked by stimulation of the vestibular apparatus are more pronounced in newborns than in adults.

3. The reaction in the new-born *after* rotation also differs from the one in adults; in: a) intensity, b) the strongly pronounced movements of head and eyes in the direction of the slow component, c) in the prominence of the slow component.

4. The quick component was absent after the rotation in sleeping infants.

5. Optokinetic nystagmus cannot be produced in new-born infants. Galebsky speaks of "rudimentary conditions of the optical nystagmus in the new-born".

6. The experiments of Galebsky show further that Bartels is right in his stating that in new-borns the reflex of the upper eyelid is elicited by bending the head downwards. Under certain conditions Bárány could arouse a definite optical nystagmus in the new-born i.e.: the child should be awake, not crying and with no intense lighting present.
Guerrier et al. (1970) performed the pendular test on 80 children, ranging in age from 0—12 years and tried to find the threshold of vestibular stimulation, which, especially in younger persons, is difficult to establish. They defined the threshold of the nystagmus as the moment when it became impossible to see an organised nystagmus (i.e. with an alternating slow and quick phase).
Until the age of six weeks they did not notice an organised nystagmus in babies, but merely a "vestibulo-ocular reflex". From the sixteenth day after birth, with the maturation of the vestibular apparatus, the nystagmus becomes more organized, but has a very high threshold. When the child grows older the threshold becomes lower and at the age of twelve the adult pattern seems to be established.
McGraw (1941) studied the changing postural and ocular behaviour of infants (0—2 years) to bodily rotation and concluded that the function of the vestibular apparatus is so complex and interwoven with other receptors that developmental factors are difficult to appraise. The changing reaction of the infant indicates an adaptation of the neural system involved. Another expression used in this respect is habituation — natural habituation — (see before).
Vestibular tests give the reaction of the peripheral vestibular apparatus to application of appropriate stimulation. The role of the C.N.S. is to conduct, to process and to interpret the information collected by the peripheral organs. It is not possible to determine the effect of an isolated stimulus in the intact organism; since the vestibular message undergoes strong influence on its way to the C.N.S., due to fresh external influences, before it can evoke a response (Gernandt 1967). The purely mechanical function of the peripheral labyrinth (cupulo-endolymphatic system) can only be demonstrated in an isolated labyrinth, in new-borns, and in a small group of people, such as the chronic seasick, who are unable to control the vestibular stimuli that reach the C.N.S. (Groen, Lowenstein and Vendrik 1952; Lowenstein 1967; Beerens 1969).
Routine messages received by the appropriate receptors are not consciously perceived, and do not, as a rule, elicit reflexes. With new stimuli this adaptation is broken down, reflex action occurs, and responses are elicited.
A very complex system is required to make the right choice from all the stimuli offered. The phenomenon of adaptation described in this respect for the sense of balance, has been known for a long time (Breuer 1875). Abels (1906) used the expression: "Gewöhnung". All the research work that has been done in connection with the vestibular system, has proved

that this adaptation is very selective, and depends exclusively on the applied stimulations. Rotation gives rise to a response decline to rotational stimuli, and less to caloric stimuli. In fact Hood and Pfaltz (1954) concluded, after subjecting rabbits to repeated rotational and caloric stimuli, that caloric responses did not give cause to any significant response decline, of the duration of the nystagmus, in contrast to the responses after repeated angular acceleration. Stimulation in one direction does not have much effect in the other direction (Collins 1964). Habituation is influenced by suggestion (Crampton and Brown 1964, 1966; Aschan et al. 1962) and can also happen in the dark. The habituation to a post-caloric nystagmus is very small, but specific for the amplitude (Mittermaier 1954).
Rotational stimuli cause a definite diminution of nystagmus reactions (Crampton and Brown 1966).
The diminution of vestibular reactions with increasing age are caused by habituation (Arslan, 1957; Minnigerode and Grohman, 1966).
It is important to keep the phenomenon of habituation in mind during clinical tests. If a specific stimulation pattern is used, such as the torsion- or parallel swing, the learning mechanism is included in the examination pattern. The sensations experienced are usually more prone to the process of habituation, than the actual reflex movements. Good examples of this are found in both the sensation cupulogram and the nystagmus cupulogram, following strong rotational stimuli (Van Egmond, Groen, and Jongkees 1948). Thorpe (1950) defines habituation as an activity of the central nervous system where the responses to certain relatively simple stimuli diminish, even those of potential value as a warning of danger, if the stimuli continue for long periods without unfavourable results.
In man the phenomenon is commonly described in figure skaters, ballet dancers, seamen, and flying personnel. They develop an immunity to the vertigo which normally accompanies excessive turning of the body in inexperienced subjects (Mowrer 1934; McCabe 1960, 1966). Both authors comment on the absence of nystagmus and vertigo in these subjects after rotational stimulation, as well as after irrigation of the ears with ice-water. The phenomenon has its origin in some central inhibitory mechanism which is not clearly understood, but which in some way suppresses the normal physiological response of the vestibular end-organ (Dix and Hood 1968, 1969). They subjected professional ballet dancers to caloric tests and found, in accordance with previous studies, that responses were either totally absent or grossly reduced.

Different results were obtained by rotational tests. The nystagmus thresholds were within the normal range in the darkness, but the strength of optic fixation was considerably raised. In these subjects there is no suppression of canal reactivity, but they develop an abnormal capacity

for maintaining visual fixation, presumably to stabilize the eyes in the presence of disturbing vestibular activity and to reinforce optic fixation. Collins (1966) obtained similar results when testing professional ice skaters i.e.: the nystagmus was strongly suppressed when their eyes were open, but a vigorous nystagmus appeared when their eyes were closed. Collins (1968) does not use the term "habituation" but prefers to regard the phenomenon as a transformation of the vestibular responses. De Wit (1953) examined normal and seasick naval personnel by means of cupulometry and it appeared that objective abnormalities of the labyrinth were present in every seasick patient investigated with this method, which consisted of a vestibular dysfunction. Krijger (1954) examined pilots also by means of cupulometry and found it desirable for pilots to possess a normally sensitive organ of equilibrium, that is an organ in which the ability of central inhibition can be demonstrated. Coles (1968), Matz and Wolfe (1971) examined naval and flying personnel and obtained minimal or no response to conventional caloric stimulation (without visual fixation). Coles repeated the test on subjects with their eyes open in a dark room, and he obtained normal responses.
It is not only the artificial stimulus that can give rise to habituation, but also the normal movements of daily life can do so. The age factor, therefore, can play an important part in this phenomenon. Groen (1963, 1965) found in new-borns (humans and animals) that the stimulation of the semicircular canals on the cupulogram in the first day of life is quite different from the pattern seen in adults. The first mentioned cupulogram is much steeper and the nystagmus reaction follows the predicted cupulo-endolymph equation of Van Egmond, Groen, and Jongkees exactly. Goetmakers (1968) found in frogs that a long-acting rotational stimulus (on a torsion swing) not only gives rise to habituation but that some habituation already exists even in the unexcited stage. Stimulation by g-forces does not seem to give rise to adaptation or habituation (Graybiel 1956; Brandt 1962). When the stimuli are applied during sleep or anaesthesia, no response decline was found (Aschan 1967; Singleton 1967; Hood and Pfaltz 1954). Guedry (1965) suggests to speak of adaptation in the sense of a decline in response during a stimulus of long duration, and of habituation if the decline follows a series of repeated stimuli.

The anatomical background for these phenomena is not clear as yet. There is an adapting process in all parts of the vestibular system (from labyrinth to cortex) but mainly in the central part (Kornhuber 1966). The efferent control of the vestibular receptors is located in the vestibular nuclei, and more specific in Deiters' nucleus (Gacek 1960; Rossi and Cortesina 1963; Carpenter, Bard and Alling 1959).
The action of the efferent part of the vestibular nerve is to diminish the susceptibility of the receptor mechanism. The connections of the vesti-

bular nuclei with the reticular substance and the cerebellum are also important (Jongkees 1969).

It is interesting to mention the studies on habituation of vestibular reflexes by Fernandez and Schmidt (1962).

They studied habituation of nystagmus by repetitive caloric stimulation in seven decorticated cats, and all animals exhibited response decline of nystagmus demonstrating that neocortex and probably basal ganglia and diencephalon are not essential for inducing habituation. There were no conclusive data regarding transfer and longlasting retention of the response decline. Acquisition of the phenomenon apparently takes place in lower centres, probably in vestibular nuclei and reticular formation of both medulla and pons or both.

Duration of nystagmus is little or not at all affected during the habituation trials. This work supports the opinion that the neural mechanism underlying habituation is a central process.

The changing reaction of the growing infant to rotation however, reflects maturation of the subcortical nuclei. The vestibular responses in new-born infants are considered to be responses from the "archaic" motor system (Ford, 1944), a name used by Gesell (1945) for the early response systems, and this "archaic" motor system is free from cerebral inhibition. Lawrence and Feind (1952) state that the vestibular system of the new-born is capable of functioning entirely on its own, since the neurons involved are amongst the earliest to become myelinated, starting at the fetal age of 20 weeks. The neurons involved in nystagmus produced by stimulation of the semicircular canals are the third, fourth, sixth, and vestibular part of the eighth cranial nerve, and the median longitudinal fasciculus. The anencephalic child in the experiment of De Kleyn and Schenk (1931), that exhibited at one week of age both components of nystagmus, suggests the ability of this "archaic" vestibular apparatus to function independently of cerebral influences, but does not prove that the cerebrum has no influence. Pendleton and Paine (1961) observed rotatory and post-rotatory nystagmus in new-borns and very young infants. They also found nystagmus when the infant was sleeping or had an anoxic or traumatic birth. The presence of a response to rotational stimuli in neonates could be explained by the possibility that this response originates at brainstem level, if it is accepted that there is little or no cerebral cortical activity. Pendleton and Paine also considered the existance of a low-level embryonal mechanism in the young infant which is replaced by a higher, specialized centre later on. Silverstein (1965) studied rotatory and post-rotatory nystagmus in 35 infants from 1—12 months old. They all had a per-rotatory nystagmus. 19 Infants from 1—5 months old showed a clear post-rotatory nystagmus, but from the 16 older infants (over six months old) only 2 showed a post-rotatory nystagmus, and 14 failed to show such a nystagmus. He states that "inhibitory" corticofugal fibres (from cortex to the vestibular nuclei)

are known to be undeveloped in new-born and young infants. This causes a bilateral facilitation of the vestibular nystagmus, as evidenced by active post-rotational nystagmus following a vestibular stimulus (manual rotation). At the age of six months, Silverstein states, apparently enough inhibitory cortico-vestibular fibres have developed to raise the threshold, and weak vestibular stimuli (such as the manual rotation that Silverstein used) do not elicit a post-rotational response.

Meadow (1968) came to the same conclusion as Silverstein after studying nystagmus during and after rotation in babies, and found that the post-rotational nystagmus disappeared after the age of four to six months. Both authors (Silverstein and Meadow), however, say that a stronger vestibular stimulus (and the "crux" of their experiment seems to lie in the very weak vestibular stimulus) such as rotation in the adult Bárány chair would, no doubt, induce post-rotational nystagmus in older infants as in adults. The manual rotation technique they used seems rather unreliable: the infant is manually rotated by a standing examiner who holds the infant facing him by supporting him under the arms with both index fingers holding his head inclined slightly forward. An assistant acts as a time keeper and gives the signal for the examiner to begin rotating on his own axis. The assistant calls "5 seconds", the time one revolution should have been completed, and without stopping the examiner completes the second revolution as the timer calls "10 seconds". It must be difficult to keep a constant time and not to rotate too fast or too slow. Further they do not mention how the "stop" is made, and as is known from cupulometry, it is the "stop" that causes the after effect. Abrupt stops give very strong reactions.

Tibbling (1969) after examining 84 children (from new-borns until fifteen years of age), obtained the same results as Rossberg (1964), Minnigerode and Grohmann (1966). She found that amplitude and eye speed of rotatory nystagmus were most intense in very young children and tended to decrease with age up to 15 years, which was the oldest age studied in their group. The older children in Tibbling's sample presumably correspond to the children over 7 years old in Zelenka and Slaninova's sample who were considered hyporeflexive. The time of the duration of the nystagmus, however, is a poor parameter of the strength of vestibular activity. This explains why Zelenka and Slaninova (1964) reported that children over seven years of age had vestibular hyporeflexia since they only took the duration of the nystagmus into consideration. Groen (1963) examined the vestibular function of a new-born (with cupulometry) on the 9th day after birth and on several occasions up to the age of three months, and found a decrease in vestibular action developing 25—60 days postpartum, because at that time inhibitory tendencies are fully developed.

Mitchell and Cambon (1969) did rotational tests on 45 neonati (1—4 days old) and found a per- and post-rotational nystagmus in the majority

of cases. They concluded that at the age of six weeks the majority of normal infants show a vestibular response to rotatory and caloric stimuli, and that this response is fully developed at 16 weeks of age. Thornval (1921) performed caloric tests on 74 babies (from 4 hours to 8 days old) and got a good caloric reaction in all the babies. The reaction was marked and instantaneous. He also noticed spontaneous eye movements in all babies before the test, similar to the nystagmoid eye movements of people under general anaesthesia. Catel (1932) studied spontaneous nystagmus in new-borns but did not mention the eye movements of new-borns studied by Bartels (1932), the so-called Doll's eye movements (head downwards→eye movements upwards; head upwards→ eye movements downwards) and eyelid reflexes (when the baby lies on his back, his eyes are closed, but when he is turned over on his tummy, he opens his eyes). Most probably these reflexes have nothing to do with the vestibular organ, and disappear during the first two months. Catel compared the spontaneous nystagmoid movements of neonati with miners nystagmus. Bartels did not think they were comparable because the miners nystagmus is more of a "flutter" in all directions, whilst the nystagmus of neonati is more like the eye movements in blind people, i.e. irregular, jerky, and somewhere between fluttering, and quick trembling. He also found that, as a result of caloric stimulation, the semicircular canals of new-borns give a longer reaction. This again we could expect to happen because habituation has not yet developed. By using as a standard to evaluate the vestibular reaction in children firstly the time-duration of the nystagmus and secondly the frequency of the nystagmus, Michishita (1967) examined—with rotatory and caloric tests—children who were in the age-range from new-born up to 15 years old. He came to the following conclusions:

a. vestibular tests in children can be done, regardless of age,

b. very faint reactions were recognized in children under 4 years old, which is, except for the neonatus, in agreement with most other researchers,

c. in children from 4 to 6 years old, the reaction values increased remarkably to almost the same level as adults, and the reactions of the children between 7 and 9 years were the highest of all.

It can be learned from the work on nystagmus tests in children that the shape of the age-function for vestibular reactivity is very complex. Beginning with infants and young children, the curve reveals a rather high reactivity level and decreases to a lower point in the second decade, followed by an increase to peak responsivity in the higher middle aged groups and finally depicting hyporeactivity again in old age when inhibitory influences from the brain get smaller again, another instance where senility recapitulates childhood.

CHAPTER III

Some experiments are described about the vestibular function in various age-groups. The results are compared and discussed.

A. Electronystagmography.

B. The caloric test (three groups of experiments).

C. Rotatory stimulation.
The cupula-endolymphe system:
   a. its reactions to rotational stimuli and more specifically to,
   b. angular acceleration,
   c. the torsion swing is discussed in detail, and also the
   d. phenomenon of directional preponderance (DP) and its clinical significance in various age groups.

Five groups of experiments with the torsion swing are described and discussed. As parameters to express the size of the vestibular responses in various age-groups we used:

A. the frequency of the nystagmus,

B. the amplitude of the nystagmus,

C. the speed of the slow phase of the nystagmus,

D. the speed of the quick phase of the nystagmus,

E. the threshold of the nystagmus for stimulation of the horizontal semicircular canals.

A. *Electronystagmography*

In the retina electric processes are always taking place, even in the dark, causing the retina to be charged negatively as against the cornea (Jongkees and Philipszoon 1964). Hence the eye is to be considered as a dipole, the electrical axis of which coincides with the optical axis. Any movement of the eye changes the field power in the region near the eye. With the nystagmograph the eye movements are recorded via these changes in the field power (see Fig. 5):

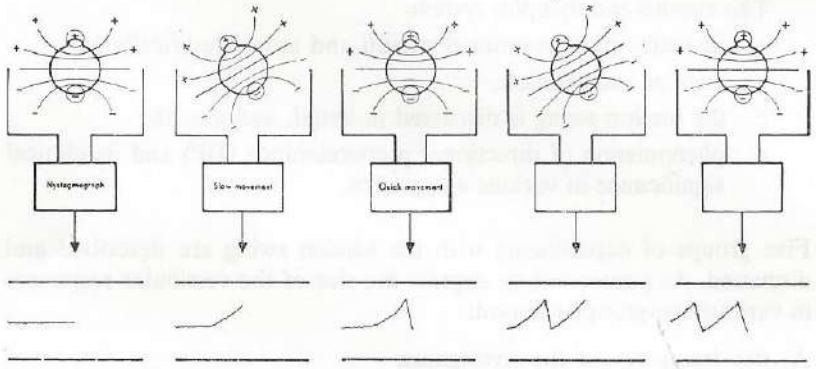


Fig. 5

In this figure the slow movement is directed towards the right and the quick movement towards the left.

The existence of the above mentioned corneo-retinal potential difference was already described by Dubois—Reymond in 1849.

Publications on electronystagmograhy appeared amongst others by: Perlman and Case (1939); Aschan, Bergstedt, and Stahle (1956); Hamersma (1957); Jongkees and Philipszoon (1960).

A great advantage of recording eye movements with electronystagmography (E.N.G.) above direct observation of eye movements by the naked eye, with or without Frenzel's glasses, is the fact that one records with the apparatus eye movements which cannot be discerned by direct observation. Furthermore it provides us with a curve, which can serve as an objective basis for discussion.

The value of this corneo-retinal potential difference at rest is between 0.25 mV and 10 mV and varies under the influence of light. As the nystagmus is recorded on a test subject with closed eyes, a change in the corneo-retinal potential due to decreased illumination is possible. Miles (1940) found a decrease of about 10 per cent after a dark adaptation of 5 minutes.

Henriksson, as well as Aschan, Bergstedt, and Stahle found the decrease insignificant. Ten Doesschate and Ten Doesschate (1956) found that "during dark adaptation the steady potential decreases slowly and

passes through a minimum value and reaches an end value which is about 90% of the previous light-adaptation level".

Horsten et al. (1963) described a new method for measurement of the CRP in rabbits and found that dark adaptation was accompanied by a continuous decrease of the CRP during a period of one hour.

Mental tension or relaxation can also cause variations. With increasing age there is a tendency for the corneo-retinal potential difference at rest to diminish (Miles 1939).

Conclusions:

If a dark room is used when eye movements are recorded with E.N.G., one should let the patients adapt themselves to the darkness for at least 20 minutes, and recalibration should take place at regular intervals. If a semi-darkened room is used, one should take care to keep illumination of the room constant (important for comparative testing) and here again the patients must be allowed to adapt themselves, in this case for about five minutes, recalibration should also be done regularly.

B. *The caloric test*

Description.

The caloric test for vestibular function is the only method which gives an indication of the sensitivity of a single vestibular organ. Brown-Séquard discovered in 1860 that syringing the ears with cold water caused giddiness, a tendency to fall, and nystagmus.

In 1906 Bárány introduced the caloric test as a clinical method, and developed the currently accepted theory for explaining the mechanisms involved. Bárány stated that, as a result of syringing the ears with water of a different temperature to that of the body, a temperature-gradient develops in the neighbourhood of the eardrum. This change in temperature is conducted to the lateral semi-circular canal via the petrous bone, and affects the temperature of the endolymph. The specific gravity of the endolymph decreases with heating and increases with cooling at the outer side of the semicircular canal. This change in the specific gravity causes a flow of the endolymph, the direction of flow depending on the position of the canal. Under optimal circumstances, with the lateral semicircular canal in a vertical position, a deviation of the cupula is caused, giving rise to the well-known vestibular phenomena. Bárány's views are supported by the following facts:

a) the direction of all vestibular reactions is always determined by the temperature of the water used and the position of the labyrinth;
b) the temperature wave that passes through the petrous bone after calorization as described by Schmaltz (1931), and the inhibition of the caloric reaction, as described by Kobrak is understandable, as is the inversion of the nystagmus sometimes seen at the end of a caloric nystagmus (Jongkees 1948);

c) the propulsion and retropulsion reactions (Fischer and Veits 1927) and the effects of bilateral syringing of the ears with water of the same temperature, are clearly described by the co-operation of the effects of the stimulation of the 6 canals. Also understandable is the intensified reaction of the lateral semicircular canals when the two ears are syringed with water of contrasting temperatures.

Further substantiating support to Bárány's hypothesis is given by the findings of Oosterveld and Van der Laarse (1968) i.e. during free fall or parabolic flight, when the influence of the force of gravity stops, no caloric reaction can be elicited. Even if a caloric reaction is elicited beforehand, it stops immediately on cessation of the g-forces. The reaction is stronger when the resultant g-force is increased and weaker when the resultant g-force is decreased to below normal (Bergstedt 1960; Kellogg and Graybiel 1967).

It is remarkable that during a long post-caloric period (up to 20 minutes or more) the already faded nystagmus (under normal g-conditions) appears again during a period of higher g-values (Oosterveld and Van der Laarse 1968). The explanation is not to be found in the deviation of the cupula, as the cupula needs some time before it returns to its resting period. It could, however, be an otolithic effect. It must be borne in mind that not only the semicircular canals, but also other parts of the petrous bone are reached and are influenced by the temperature wave, and it is therefore likely that the perception of a changed situation (Grahe 1923, 1927) is dependent on otolith stimulation (Jongkees 1949). Under the influence of longlasting strong caloric stimulation even hearing may be changed (Voogd 1946), because the temperature gradient reaches the cochlea and so can cause diplacusis.

The electronystagmographic method of investigation (E.N.G.), where eye movements are recorded, makes an accurate quantitative analysis of the caloric test possible, the main advantage being that a permanent record can be obtained. In the routine caloric test recorded by means of E.N.G., the frequency and duration of the nystagmus, as well as the maximum velocity of the slow phase, are calculated. In the early phases of E.N.G., investigators occupied themselves primarily with the study of the quantitative parameters, and in particular with the determination of the normal values of these parameters in normal subjects (Aschan 1955; Hamersma 1957; Maas 1960; Jongkees and Philipszoon 1964). The basic standard, bilateral, both cold and warm stimulation-technique for the caloric test was established more early (Thornval 1917; De Kleyn 1927; Fitzgerald and Hallpike 1942; Jongkees 1948).

The following technique is used in our first experiments. The two ears are alternatively syringed during 30 sec, with 250 cc of water of 7° C above, and of 7° C below the average body temperature, with the subject in the supine position, and his head flexed forward over an angle of 30°. A 20 minutes interval is allowed between the irrigations, in order

to avoid interferences of previous reactions (Jongkees 1949; Hamersma 1957; Oosterveld and Van der Laarse 1968). The tests are performed in a semi-darkened room, with the subject's eyes closed (Aschan et al. 1956; Anderson et al. 1958; Jongkees 1960).

Response number 1 represents the eye movements, especially the maximum velocity of the slow phase after syringing the right ear with water of 30° C.

Response number 2 represents the eye movements, especially the maximum velocity of the slow phase after syringing the left ear with water of 30° C.

Response number 3 represents the eye movements, especially the maximum velocity of the slow phase after syringing the right ear with water of 44° C.

Response number 4 represents the maximum velocity of the eye movements, especially of the slow phase after syringing the left ear with water of 44° C.

The sum of these four values (V) (1+2+3+4) is used to express the caloric excitability.

The normal subjects selected for the investigations had to conform to the following criteria:

a) to be between 10 and 90 years of age (we excluded subjects under 10 and over 90 years of age, because it was very difficult to obtain young children and very old people for test purposes, and the ones we got we rather subjected to the less complicated, and more enjoyable torsion-swing test),
b) to be representative of both sexes,
c) to be in good physical health, i.e. a case history free of pathology, especially as far as the ears were concerned,
d) complete absence of pathological spontaneous, or positional nystagmus,
e) absence of pathological labyrinth predominance, or directional preponderance,
f) the subject had to be awake and alert during the test,
g) drugs or alcohol had to be avoided for at least 48 hours preceding the tests,
h) the subjects had to show normal audiological findings.

Of the 400 people who were willing to submit themselves to the experiment, 250 subjects who complied with the above-mentioned criteria were selected.

Recording of the nystagmus

The nystagmus is recorded with an Elema mingograph, EM 84, completed with preamplifiers type EMT-12.

After the skin has been cleaned, two Siemens electrodes are attached with adhesive rings to the outer canthus of the eyes. A third electrode

serving as an earth electrode is placed medially on the forehead. A contact paste (contactine, Siemens A.G., Erlangen) is used in order to get a better conduction.
The leads are so arranged that an eye movement to the left is always recorded as a downward deviation on the recording, and vice versa (Hamersma, 1957).

Calibration

Calibration was carried out by asking the patient to look alternately at two illuminated spots at three metres distance and arranged in such a way as to cause a rotation of the eyes through an angle of exactly 20°. The degrees of rotation of the eye are thus translated into milimetres deviation in the recording.

Diagram of the subdivision of the 250 subjects into seven groups according to their age. The number of individuals in each group is given (N). V is the total value of the four responses, representing the eye movements, especially the maximum speed of the slow phase after syringing with water of 30° C and 44° C, for all the members of the group added together and the value $\frac{V}{N}$ is recorded on the ordinate of Fig. 1, and the age-group on the abscis.

TABLE I

Age-group	Number (N)	Age	Value (V) 1+2+3+4	$\frac{V}{N}$
I	10	10–20	999	99
II	27	21–30	3011	111
III	37	31–40	4421	119
IV	41	41–50	4145	101
V	54	51–60	5116	95
VI	47	61–70	4433	94
VII	34	> 71	2831	83

We noticed a steep increase in vestibular excitability in the first groups, reaching a maximum in the third group. From hereon there is a slow decrease in the vestibular excitability, coming to the lowest value in the last group.
It has been discussed (Stahle 1956) whether cold or hot syringing may be regarded as equivalent stimuli, giving equally long periods of nystagmus. Lorente de Nó (1936), Fitzgerald and Hallpike (1942); McNally, Stuart, Jamieson and Gaulton (1948); Jongkees (1948); Hallpike, Harrison, and Slater (1951); Schierbeek (1951); and Wodak (1953) reported nystagmus to persist longer after cold syringing; Jongkees (1948) claims that this is a vaso-motor effect. He succeeded in reducing nystagmus duration following cold stimulation by local administration of a vaso-

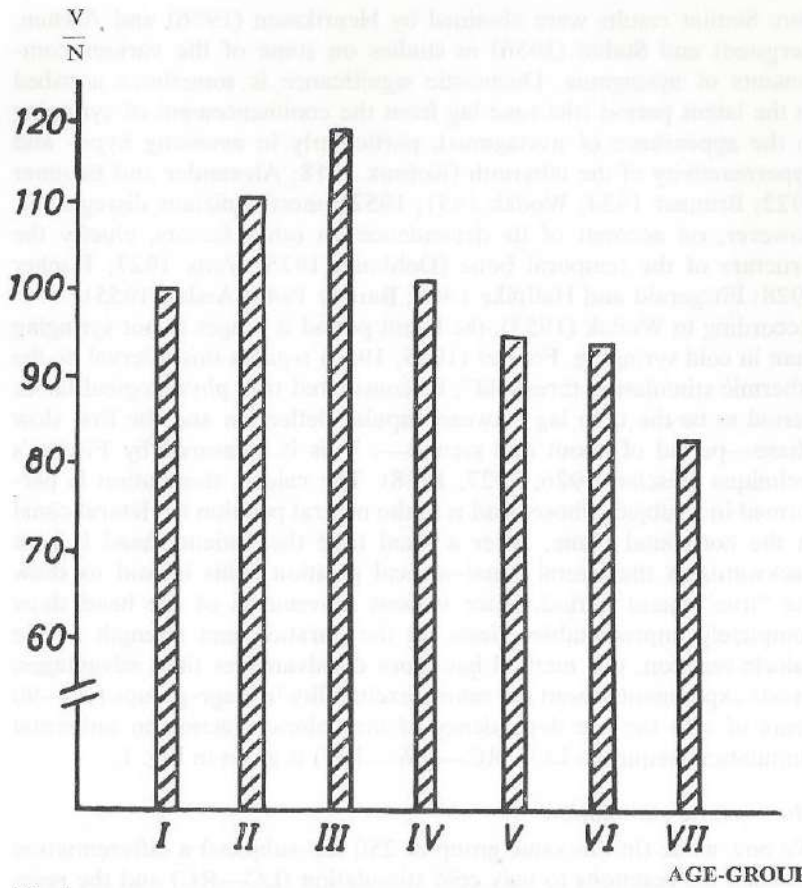


Fig. 1
Caloric nystagmus and age.
Caloric nystagmus and age measured in a group of 250 subjects from 10–90 years old, subdivided into seven groups (see Table I, page 44). The sequence of irrigation was Left Cold–Right Cold–Right Warm–Left Warm. V is the total value of the four responses, representing the maximum speed of the slow phase after syringing with water of 30° C and 44° C, for all the members of the group together. N is the number of individuals in each group. $\frac{V}{N}$ represents the mean maximum eye-speed of the slow component per group.

dilator (amyl nitrite) to counteract vasoconstriction. The drug had no effect on the hot response since dilatation was presumably already maximal. Jongkees further confirmed the importance of local vascular influences on the caloric response with demonstrations of the vaso-constrictive effects of procaine hydrochloride, injected into the wall of the outer meatus. Aschan (1955) showed that the mean maximum eye-speed in the slow phase was the same after both cold and hot caloriza-

tion. Similar results were obtained by Henriksson (1956) and Aschan, Bergstedt and Stahle (1956) in studies on some of the various components of nystagmus. Diagnostic significance is sometimes ascribed to the latent period (the time lag from the commencement of syringing to the appearance of nystagmus), particularly in assessing hypo- and hyperreactivity of the labyrinth (Kobrak 1918; Alexander and Brunner 1922; Brunner 1924; Wodak 1951, 1952); most clinicians disregard it, however, on account of its dependence on other factors, chiefly the structure of the temporal bone (Dohlman 1925; Veits 1927; Fischer 1928; Fitzgerald and Hallpike 1942; Barbey 1943; Arslan 1955).
According to Wodak (1953), the latent period is longer in hot syringing than in cold syringing. Frenzel (1925, 1954) regards this interval as the "thermic stimulation threshold"; he considered true physiological latent period to be the time lag between cupular deflection and the first slow phase—period of about one second—. This is measured by Fischer's technique (Fischer 1926, 1927, 1928). The caloric stimulation is performed in a subject whose head is in the neutral position i.e. lateral canal in the horizontal plane. After a fixed time the patients head is bent backwards in the lateral canal-vertical position. This is said to show the "true" latent period. Since various movements of the head show completely unpredictable effects on the duration and strength of the caloric reaction, this method has more disadvantages than advantages.
In our experiments about the caloric excitability in 7 age-groups (10—90 years of age) the age dependency of the caloric reaction to bithermal stimulation (sequence LC—RC—RW—LW) is given in Fig. 1.

Monocaloric stimulation

We now made (in this same group of 250 test-subjects) a differentiation between the reactions to only cold stimulation (LC—RC) and the reactions resulting from only hot stimulation (Fig. 2).
From this figure it is learned that the distribution of responses to warm water according to the age of the test-person shows little change with increasing age, but responses to cold water do show a small but clear change decrease with increasing age. The older subjects give a disproportionally stronger response to the warm irrigations than to the cold. This agrees with the findings of Bruner and Norris (1971) and Brookler and Pulec (1970) (see before). It is still a question whether the influence here is local vascular or if there is a factor associated with repeated testing to which old people are more sensitive than the young (a response enhancement instead of the response decline in the young group).
Most likely is the influence local vascular, when we assume that with increasing age there is a gradual diminution in blood flow to the labyrinth due to vascular narrowing. Syringing with hot water brings about vasodilatation and an improved blood supply, which elevates the neural

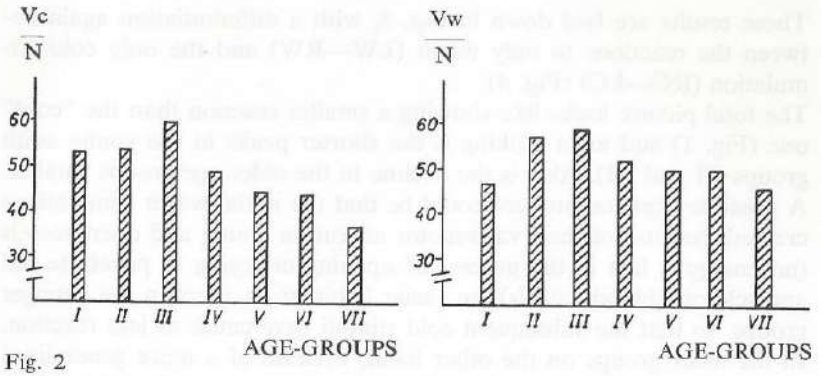


Fig. 2

Caloric nystagmus and age. See Legend Fig. 1. (See table I, page 44). The left diagram shows the results after only cold stimulation (sequence Left Cold–Right Cold) and the right diagram shows the results of only warm stimulation (sequence Right Warm–Left Warm). VC in the left diagram is the total value of the two responses representing the maximum speed of the slow phase after syringing with water of 30° C, for all the members of the group together. VW in the right diagram is the total value of the two responses, representing the maximum speed of the slow phase after syringing with water of 44° C, 20 minutes after the cold stimulation, for all the members of the group together.

$\frac{VC}{N}$ represents the mean maximum eye-speed of the slow component per group.

$\frac{VW}{N}$ represents the mean maximum eye-speed of the slow component per group.

discharge of the stimulated ampulla over that resulting solely from cupular bending. In the middle-aged ear this vasodilatory action is more marked,—because the vessels are partially narrowed—than in the ear of a young person where they are fully patent. To rule out an eventual influence of the order of stimulation, we tested another group of test-persons, applying the hot stimulation prior to the cold one (LW—RW—RC—LC). This group consisted, according to the following diagram, of 84 subjects, subdivided into seven age-groups. As in the former group, the number of individuals in each group is given (N), and V and $\frac{V}{N}$ have got the same meaning as in the diagram of the above mentioned "cold" group.

TABLE II

Age-group	Number (N)	Age	V 4+3+2+1	$\frac{V}{N}$
I	10	10–20	855	85
II	18	21–30	1619	90
III	10	31–40	762	76
IV	12	41–50	979	81
V	13	51–60	1177	90
VI	11	61–70	979	89
VII	10	> 71	881	88

These results are laid down in Fig. 3, with a differentiation again between the reactions to only warm (LW—RW) and the only cold stimulation (RC—LC) (Fig. 4).
The total picture looks like showing a smaller reaction than the "cold" one (Fig. 1) and most striking is the shorter peaks in the young adult groups (II and III). Also is the decline in the older age-groups smaller. A possible explanation here could be that the initial warm stimulations created, because of their vaso-motor action on young and open vessels (no energy is lost in the process of opening or trying to penetrate old and sclerotic blood-vessels), an easier habituation-effect in the younger groups, so that the subsequent cold stimuli gave cause to less reaction. In the older groups on the other hand, because of a more generalized atherosclerosis and narrower labyrinthine vessels, this habituation-phenomenon could not play such an important role.

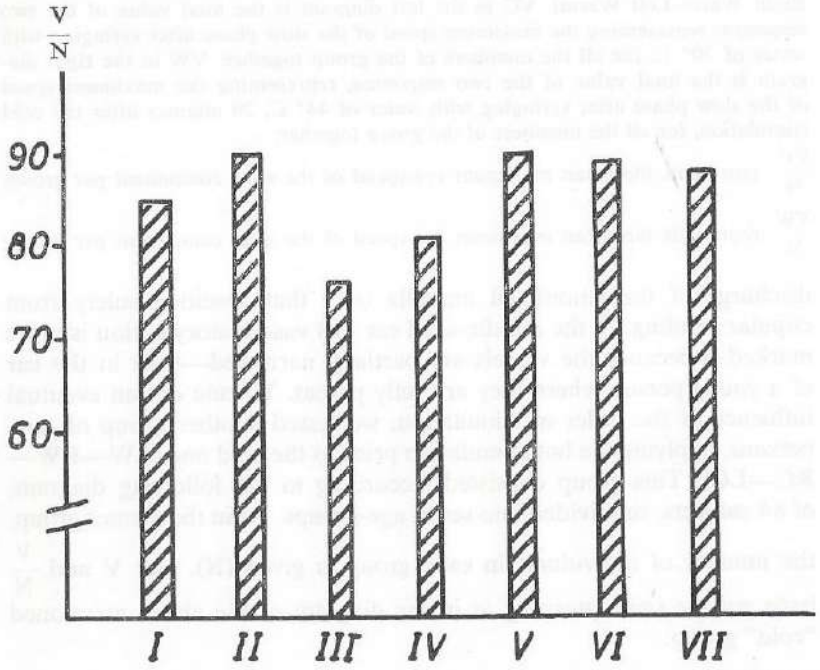


Fig. 3
Caloric nystagmus and age. See also Legend Fig. 1.
Caloric nystagmus and age measured in a group of 84 subjects from 10–90 years old, subdivided into seven groups (see Table II, page 47). The difference with the tests mentioned under Fig. 1 and Fig. 2 is that the sequence of stimulation was Left Warm–Right Warm–Right Cold–Left Cold.
V is the total value of the 4 responses, representing the maximum speed of the slow phase after syringing with water of 44° C and 30° C, for all the members of the group together.

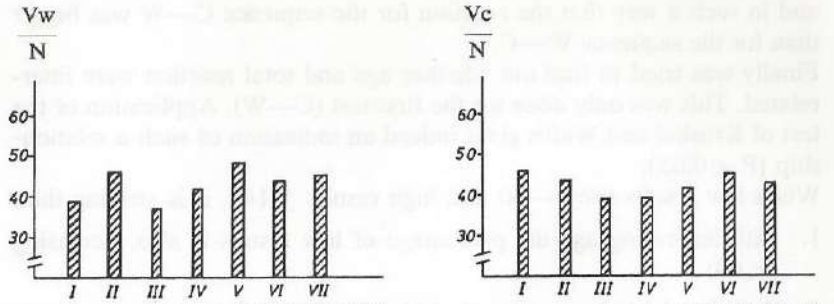


Fig. 4
Caloric nystagmus and age. See Legend Fig. 2 and 3. (See Table II, page 47). The left diagram shows the results after only warm stimulation (sequence Left Warm–Right Warm) and the right diagram shows the results of only cold stimulation (sequence Right Cold–Left Cold).
VW in the left diagram is the value of the 2 responses representing the maximum speed of the slow phase after syringing with water of 44° C, for all the members of the group together.
VC in the right diagram is the total value of the 2 responses representing the maximum speed of the slow phase after syringing with water of 30° C, 20 minutes after the warm stimulation, for the same members of the group together.

The other conclusion we can make is that, in agreement with Collins's (1965) view, repeated caloric stimulation will produce a response decrement, and this will be a greater decrement if the initial stimulation is a warm one (Grahe 1932; Lorente de Nó 1936; Hallpike 1942). We further noted, in agreement with Hart (1969) that the cold-water irrigation induces a stronger nystagmic response than the hot-water irrigation does. The age decline in the higher age-groups (as seen in the total figures 1 and 3) shows the general age-effect, caused by atherosclerosis and reduction of neural excitability (loss of central inhibitory control).

Results of statistic analysis of the results of the caloric test.

This analysis was done by Ir. A. A. M. Hart of the Laboratory of Medical Physics, Amsterdam.
In the first place an investigation was made to find out whether a difference existed between the reaction on the cold and on the warm stimulation. The analysis was made by means of the test for symmetry of Wilcoxon, and with this test an indication of such a difference could be demonstrated only for the age-group VI (61—70) of the first experiment, the C—W stimulation with the differentiation in C and W alone — see Fig. 2 — ($P < 0.05$ according to Table J in "Inleiding tot de medische statistiek, deel I, H. de Jong, Leiden 1958).
Then was checked whether a difference existed between the total reactions of the C—W and W—C tests (Fig. 1 and 3). The test for symmetry of Wilcoxon gave indeed the indication of such a difference for the age-groups (21—30 (II) and 31—40 (III)), ($P < 0.025$ resp. $P < 0.005$)

and in such a way that the reaction for the sequence C—W was bigger than for the sequence W—C.
Finally was tried to find out whether age and total reaction were interrelated. This was only done for the first test (C—W). Application of the test of Kruskal and Wallis gives indeed an indication of such a relationship ($P < 0.05$).
When low results are 0—60 and high results >141, it is striking that:

1. with increasing age the percentage of low results is also increasing (<60),
2. there is a fairly large amount of high results (>141) in the age-group 31—40 (III).

C. *The rotatory stimulation*

The cupula-endolymphe system

a. The physics of the reactions to *rotational stimuli* on the semicircular canals are discussed by Van Egmond, Groen, and Jongkees (1948). From the work of Steinhausen (1931) and Dohlman (1935) can be concluded that the endolymphe of canal and utricle forms a close fluid ring with a density and a viscocity nearly that of water. The fluid ring is kept in place by a hermetically sealing valve, the cupula, which can move frictionless in its dome. Cupula and endolymphe form together an inertia system with an equilibrium position. If this system is submitted to a constant angular acceleration αrad/sec^2, a pressure difference p dynes/cm^2 over the cupula will be generated. The pressure difference will force the cupula into a deflected position where its restoring force will be in equilibrium with the inertial force. By measuring the changes in the frequency of the action potentials of the ampullar nerve in the ray (raja clavata) Groen could prove that the deflection is proportional to the force (pressure) within wide limits, in both directions (Groen; Lowenstein 1952). This is also valid for the frog (Ledoux 1949), but within a narrower range. If a canal is plugged, a once deflected cupula will stay deflected indefinitely long whereby the activity in the isolated nerve will remain constant. This proves that the cupula of the frog does not leak and that adaptation phenomena are absent in its peripheral organ. If the plugging is removed the cupula will return to equilibrium position according to an exponential law. This can also be demonstrated by bringing about a sudden stop following a long period of constant angular velocity of e.g. 36°/sec; constant the decay appears to be 40 sec. From these observations it seems plausible to ascribe a constant directional momentum Δ and a constant frictional momentum Π to the cupula-endolymphe system. The ratio $\frac{\Pi}{\Delta}$ determines the rate of decay (c.f. 40 sec). It can now be said that the semicircular canals react to a linear

second order differential equation of the heavily damped torsion pendulum (Van Egmond, Groen, and Jongkees 1948).
Whenever a vestibular stimulus lasts too long, inhibitory tendencies are present, which is called adaptation (Groen). This central inhibition would reduce the activity in such a way that the decay can take place according to an exponential law with a smaller decay constant than belongs to the peripheral organ. One possible explanation is that inhibition goes proportional to the momentary activity, or to that one which occurred in a certain time interval before. The genuine motion-sick individuals apparently lack the capacity for inhibition. Their cupulograms are extraordinary steep, showing the lack of inhibition (De Wit 1953; Krijger 1954). Another source of interference with the simple pendulum behaviour is the tendency to pattern-formation (Groen 1957, 1963, 1965). Any normal test subject will—under the conditions of periodic stimulation—build up the counter part of that stimulus form in a pattern centre, which must be located somewhere in the central nervous system. This counter part, the pattern copy, will act in such a manner, that it will take care of all temporary adjustments of equilibrium, modified eventually for small deviations of the true stimulation, and that it reduces or even abolishes the influx of the vestibular signals to the cortical area where the sensations are presumably located. This hypothesis has been formulated to explain the adaptation of a normal individual to the motion of a ship (Nieuwenhuysen 1958). It states that during the first period aboard ship, a pattern of the ships motion is built up, which goes on functioning even when the sailor goes ashore and needs it no longer, thus giving him a continuing sensation of the moving ship, be it in a reversed way provoked by the pattern copy which is the counter part of the original movement.
These pattern phenomena have been noticed since long; they e.g. interfere with the sensations a test subject has when submitted to a periodic stimulus—oscillation—on a torsion swing. If the swing is set into motion and left free thereafter, the declining amplitude of the real stimulus and the pattern resulting as a consequence of the first swingings, will interfere in such a way that the test subject sometimes will not feel a swinging to one side whereas the movement to the other side will be perceived clearly. In a next phase the subject can be insensitive for the other direction. These results are probably brought about by an interference of stimulus and pattern activity out of step.
The inhibitory tendencies are not constant, they depend upon many factors such as previous stimulation and condition of the individual. We think that the age-factor also plays an important part in all these phenomena.

b. The actual stimulus for the semicircular canals is change of *angular speed*. To a far smaller degree, they might also be sensitive to linear

accelerations (in any case 200 times less than the otolith-organs), but this has never been proved (Jongkees and Groen 1946). Steinhausen (1932) found that cupula movements are caused by rotatory stimuli. This happens because of the inertia of the fluid-ring in the canals. After accelerations, when a constant rotatory movement follows, the cupula slowly returns to the original position by its own elasticity.
The deviation of the cupula is the cause of the sensations and reactions observed. The extent and duration of the sensations and reflexes are dependent on the magnitude and duration of the deviation of the cupula.
It is important for the rotatory stimulus to be applied accurately in the plane of the canal to be examined (Fischer and Wodak 1922; Veits 1931; Woletz 1932). If stimulation is applied in intermediate planes, confusing combinations of the reactions from the various semicircular canals may be obtained (Ek, Jongkees, and Klijn 1960).
The examination of the cupula function has been changed and refined during the last decades. Cupulometry is a good example here of (Van Egmond et al. 1948, 1952).
The rotational test is in one aspect imperfect for clinical use, in that the left and right semicircular canals are tested together and if one side is sick it is difficult to decide which is the affected side. This might be done following Ewald's second law, that the reactions after rotation to the left are caused by the right labyrinth and vice versa. Ewald's observations are only true for major stimuli: rotation of more than 50°/sec (Ledoux 1958, 1967) or more than 60°/sec (Groen, Lowenstein, and Vendrik 1965) but not for minor stimuli. Furthermore it is likely that Ewald's law is only true for acute, and not for chronic conditions, where compensation could have taken place in the central nuclei of the vestibular system. It is easy to determine such compensation in the cupulogram. Using small stimuli one finds that the sensitivity of the vestibular system reverts to normal again (i.e. being compensated). However, with stronger stimulation, this compensation does not take place, as the "load-threshold" is lowered (Hulk and Jongkees 1948).

Most authors nowadays consider the cupula-endolymphe system as a heavily damped torsion pendulum (Steinhausen 1931; Van Egmond, Groen, and Jongkees 1949; Groen, Lowenstein, and Vendrik 1952). The estimation of the period of the cupula-endolymphe system can be established by means of sinusoidal stimulations (on a torsion swing) of different period value. When there is resonance between the cupular deflection and the pendular movement, the period of the cupula-endolymph system and that of the imposed sinusoidal movement have the same value. In this case there is a 90° difference of phase.

Van Egmond, Groen, and Jongkees (1948) have established the equation of the functioning of the cupula-endolymphe system (see earlier).

c. *Torsion swing*

The torsion swing is known in vestibular physiology since Mach (1875). Van Egmond, Jongkees, and Groen (1943) used it for the evaluation of their equation of canal function.
Since the introduction of nystagmography the torsion swing has been used for clinical test of the semicircular canals (Greiner et al. 1961; De Boer et al. 1963). In a very short time a series of nystagmus beats is provoked in both directions with decreasing intensity of the stimulus.

1. As long as the amplitude of the swing (Janeke 1968; Clemens and Festen 1970) stays within 5° about, most human test-subjects show merely a pure sinusoidal eye movement without nystagmus beats.

2. For larger amplitudes, nystagmus intercepts the ocular movement, forcing the eyes to oscillate during one half of the cycle in a narrow margin bounded on one side by the eye centre position, whereas the eye moves over to a comparable margin on the other side during the next half of the cycle. The results can be analysed into a pendular movement and a series of nystagmus strokes.

3. The margin within which the eye executes its nystagmus strokes is not bounded by the theoretically straight centre position line, but by a sinusoid. The fast nystagmus strokes hit against this sinusoid, the slow strokes move away from this undulatory line. From this it is concluded that the eye changes its resting position periodically with the pendular movement. This was already demonstrated by Buys (1924) and Borries (1926) in nystagmus recordings.

The per-oscillatory nystagmogram on the torsion swing consists of periodical eye movement on which nystagmus is superimposed. This periodic movement is primarily of vestibular origin (Clemens and Festen 1970).
Torsion-swing stimulation of normal test subjects reveals that as soon as nystagmus has disappeared because of habituation, the pure periodic movement may persist, but it has to be mentioned that also this can subside.
These periodic eye movements are ascribed by Clemens (1970) to pattern centre activity. Groen (1957) observing recordings during post-oscillatory periods for 15-30 minutes, pointed to the presence of an afference copy, active in the central nervous system, a copy formed in the per-oscillatory period, comparable to the pattern in the pattern centre from his well known theory, and thinks that the torsion swing, apart from the advantages we are mentioning later, can be used for the study of pattern-centre activity and its possible connection with habituation.
We want to run ahead of one more advantage of the torsion chair, in that a directional preponderance can easily be detected with its aid, and there also seems to be an age factor connected to this phenomenon.

d. *Directional Preponderance (D.P.)*

The significance of D.P. of the nystagmus evoked by vestibular stimulation has been investigated for over 50 years (Eviatar and Wassertheil 1971). Former workers (Fitzgerald and Hallpike 1942) concluded that D.P. might be of central as well as of peripheral origin. The finding as such is small, and without any supportive clinical data is disregarded by some clinicians (Jongkees 1948, 1949, 1966; Maran 1966). Eviatar and Wassertheil (1971) examined the clinical records of 1101 patients, who all had electronystagmographic examinations. They had an age-range of 5—80 years, and their final diagnosis varied from vestibular disease to brain tumours, to psycho-physiologic complaints and many other diagnostic conclusions in between. Bithermal caloric tests (30° C and 44° C) were performed and Jongkees' formula was adopted to determine the D.P. (Jongkees et al. 1962).

Out of these 1101 patients examined, 246 were found to have D.P. It was demonstrated with this sample that, although D.P. was significantly connected with central nervous system disease, the degree of associations was too small to render it a specific pathological sign. This may explain why directional preponderance is not generally accepted in practice as a meaningful diagnostic result. However, when the existence and direction of spontaneous or positional nystagmus is considered, the association between directional preponderance and central disease increases for the patients who do not have a spontaneous or positional nystagmus, or whose nystagmus is directed to the opposite side of the directional preponderance. This finding seems to agree with the theories that a directional preponderance might be an expression of an existent spontaneous nystagmus which remains latent (Jongkees 1953). This he bases upon the fact that in patients with a pathological process a directional preponderance may change in a spontaneous nystagmus and vice versa.

It is Hamersma's (1957) experience that a directional preponderance is usually accompanied by a spontaneous or a provocable nystagmus. The quantitative contribution of a spontaneous nystagmus to the production of the phenomenon of directional preponderance can not always be excluded by arithmetical calculations. It is worth while to consider the possibility whether a pathological directional preponderance does exist when a spontaneous or provocable nystagmus has been excluded, because this phenomenon also exists in normal individuals. In their study Eviatar and Wassertheil (1971) find that directional preponderance becomes meaningful when the age of the patient is considered. The younger the patient the greater the association between a directional preponderance and central disease. Practically, this association may be diagnostic before the age of 30, suggestive from 30—50, and completely nonsignificant afterwards. Physiologically, this may be explained as follows: Relative ischemia of nystagmogenic areas in the brain due

to minor cerebro-vascular insufficiency is probably prevalent in the higher age-group. While these minor ischemic changes may be considered as a normal ageing process without disturbing other functions, they are enough to create a minor imbalance between the different nystagmogenic areas. This imbalance is responsible for a subliminal nystagmus that may reveal itself only under elimination of inhibitory factors such as light and fixation. Under such conditions, it may appear as a spontaneous or positional nystagmus. This type of nystagmus may also express itself by a directional preponderance, in the same direction as the existent nystagmus, under the same conditions of elimination of inhibitory factors. In younger subjects where atherosclerosis and other ageing factors are not prevalent, this type of "benign" directional preponderance is rare. Here a D.P. is probably the result of a definite irritation of a nystagmogenic area, usually in the brain, but sometimes an acute peripheral disease may be the cause. When a D.P. is in the opposite direction of a spontaneous or positional nystagmus, it is certainly not an expression of this nystagmus. It may be interpreted as a result of pathologic stimulation, that can overpower and reverse the direction of an existent latent nystagmus. This may explain why, regardless of age, cases with a D.P. in the opposite direction of the positional nystagmus or without any positional nystagmus showed a significantly higher percentage of pathology. No correlation was found between D.P. and labyrinthine disease. This finding may be interpreted (according to Eviatar and Wassertheil 1971) that although in sporadic cases a peripheral labyrinthine injury may be the reason for a D.P., D.P. by itself does not imply that such a lesion is present. To provide a meaningful interpretation of D.P. in regard to pathology in an individual case, we shall still need the skill and the experience of the clinician.

On the previous page we introduced the *torsion swing* and mentioned two of its advantages:

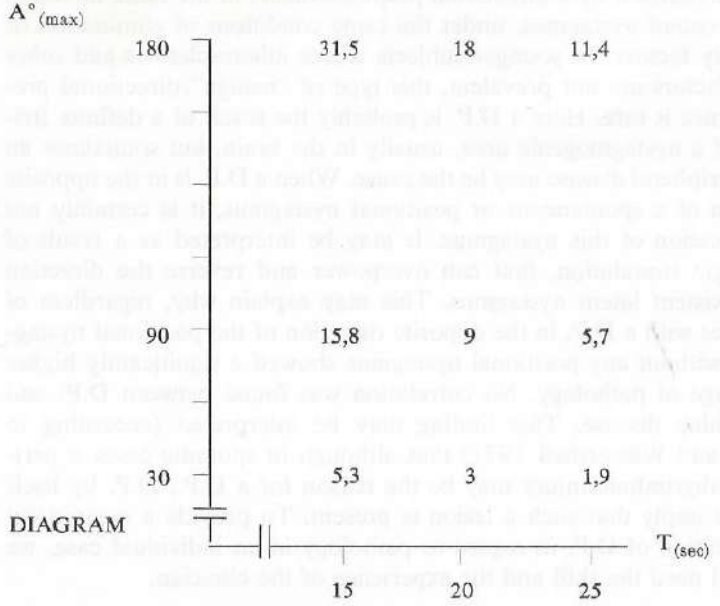
1. its use for the study of pattern-centre activity,
2. its use in the detection of directional preponderance.

The torsion swing used in our experiments consists of a chair suspended from the ceiling by means of a vertical iron bar. The chair movement is exponentially damped after an initial deviation by hand.

I. *Duration of the period*

Greiner et al. (1961) got the best results with periods of 20 seconds. Hennebert (1965) found that with periods lasting longer than 44 seconds the angular acceleration did not give the appropriate vestibular response. Most authors got the best clinical results with periods varying between 15 and 25 seconds and with periods between 18 and 20 seconds no disturbing habituation is seen.

For this reason in most of our torsion swing experiments we used periods of twenty seconds. This made the calculations easier, because with a starting angular deviation of 180° the maximum acceleration is 18°/sec², with an angular deviation of 90°, the maximal acceleration is 9°/sec², and with an angular deviation of the torsion swing of 30° the maximum acceleration is 3°/sec². For calculations, see diagram.
For clinical use it is very important to keep a constant period. In our case we also obtained a fixed number of movements.



DIAGRAM

Variations of the max. acceleration (°/sec²) as a function of the amplitude ($A_{(max)}$ in °) for periods of 15, 20 and 25 seconds.

II. *Influence of weight*

The characteristics of the period can be strongly modified by the weight of the test subjects. We overcame this problem by adjusting movable weights, placed on both sides underneath the chair (more centrally or more laterally), by adding some (in case of small children), or by taking away a few (in the case of heavy adults), with the intention to make the weight distribution equal in all tests.
The chair is put into action by hand with an initial deviation, clockwise, of 180° from its resting position. After being released it makes its first rotation counter clockwise: the first part is active during half a turn of 180°, until the moment of return at its resting position (0°) with maximum speed and follows its course counter clockwise until reaching the 180° position, or rather —170° (10° loss for the damping factor). Now

the movement goes on clockwise, accelerating until reaching the 0° position where the acceleration changes its direction until a deviation of about 160° is reached. This movement of going and coming back has a duration of 20 seconds. On account of damping of the torsion swing, the maximum amplitude decreases with each period. The maximum angular speed (in °/sec) is about a third of the corresponding maximum amplitude.
The angular acceleration (in °/sec²) can be expressed as a value of about one tenth of the maximum amplitude. An improved version of the torsion-swing chair is described by Janeke, Janeke, and Oosterveld (1971). It is of a simple, mobile, and inexpensive construction.
The advantages of the torsion-swing chair are:

1. it is a quick method to investigate the sensitivity of the vestibular system to a rotational stimulus,
2. it is an easy method to establish whether there is a directional preponderance of the provoked nystagmus (Martin 1968; Oosterveld 1965) (about D.P. see before),
3. it is desirable to do the torsion-swing test to complete a vestibular examination, especially if there is a caloric inexcitability of both labyrinths,
4. it is a simplified method to gain information on the vestibular function in children, as the mothers can hold their infants in their arms on the chair,
5. it is a method to evaluate the effects on anti-motion sickness drugs on the vestibular function in animals as well as in human beings (Jongkees; Philipszoon 1960; Martin and Oosterveld 1970; Oosterveld 1965; 1967),
6. the evolution of the compensation phenomenon of Ruttin (1911, 1912) was studied with the aid of the torsion swing (Van de Calseyde 1971). Frequency nystagmograms were done on patients after unilateral labyrinthectomy for Ménière's disease,
7. its use for the study of pattern-centre activity (see before).

III. *Examination technique*

All tests with the torsion-swing chair were performed in a semi-darkened room with the test person sitting with his head flexed forward over 30°, and his eyes closed.
During most of our tests we kept the test persons alert by asking them simple questions or letting them do mental calculations.

IV. *Recording of nystagmus*

The nystagmus is recorded with an Elema mingograph EM 84, I used the same technique for putting on the electrodes and the same technique for calibration as mentioned before under "caloric test".

A. Frequency of the nystagmus

Buys (1925) expressed the opinion that the frequency is the physiologic base of the nystagmus and for Montandon (1965) it was the only real quantitative parameter.

The frequency is the number of beats in a certain time unit.

The frequency of the nystagmus varies with the value of the maximum angular acceleration. It is easy to count the number of nystagmus beats during a certain time unit in the nystagmogram. In normal subjects the difference between the number of beats to the right and to the left is not more than 10% (Greiner et al. 1961). This difference between the total number of nystagmus beats to the left and the total number of beats to the right during the first ten swingings of the torsion swing is expressed as a percentage of the total number of beats

in the formula $\frac{(L-R)}{(L+R)} \times 100\%$

(Jongkees, Maas, and Philipszoon) (L = left; R = right).

The mean and standard deviation of the difference between left- and right beating nystagmus in 80 normal subjects were calculated (De Boer, Carels, and Philipszoon 1963). The mean was +1.2%. The reason that this is not zero and that this figure has a positive sign they explained by the fact that the first swinging was always to the left, which makes the total size of the stimulation provoking nystagmus to the left greater than the total stimulus for nystagmus to the right.

The standard deviation was 11%. They proposed to call a value for the difference between left- and right beating nystagmus lying beyond +23% and —23% (double standard deviation) a pathological directional preponderance, as less than 5% of normal subjects have such a directional preponderance.

In the following experiment on the torsion swing is shown that there is a variation in the frequency of the nystagmus depending on the age of the subject.

We examined a group of 395 people who, according to their age were subdivided into 9 groups:

TABLE III

Age-group	Number	Age	Mean frequency of the nystagmus	
			L	R
0	11	1–10	17	15
I	15	11–20	28	26
II	54	21–30	27	27
III	55	31–40	27	27
IV	73	41–50	29	27
V	97	51–60	29	29
VI	60	61–70	28	27
VII	23	71–80	28	27
VIII	7	> 81	24	24

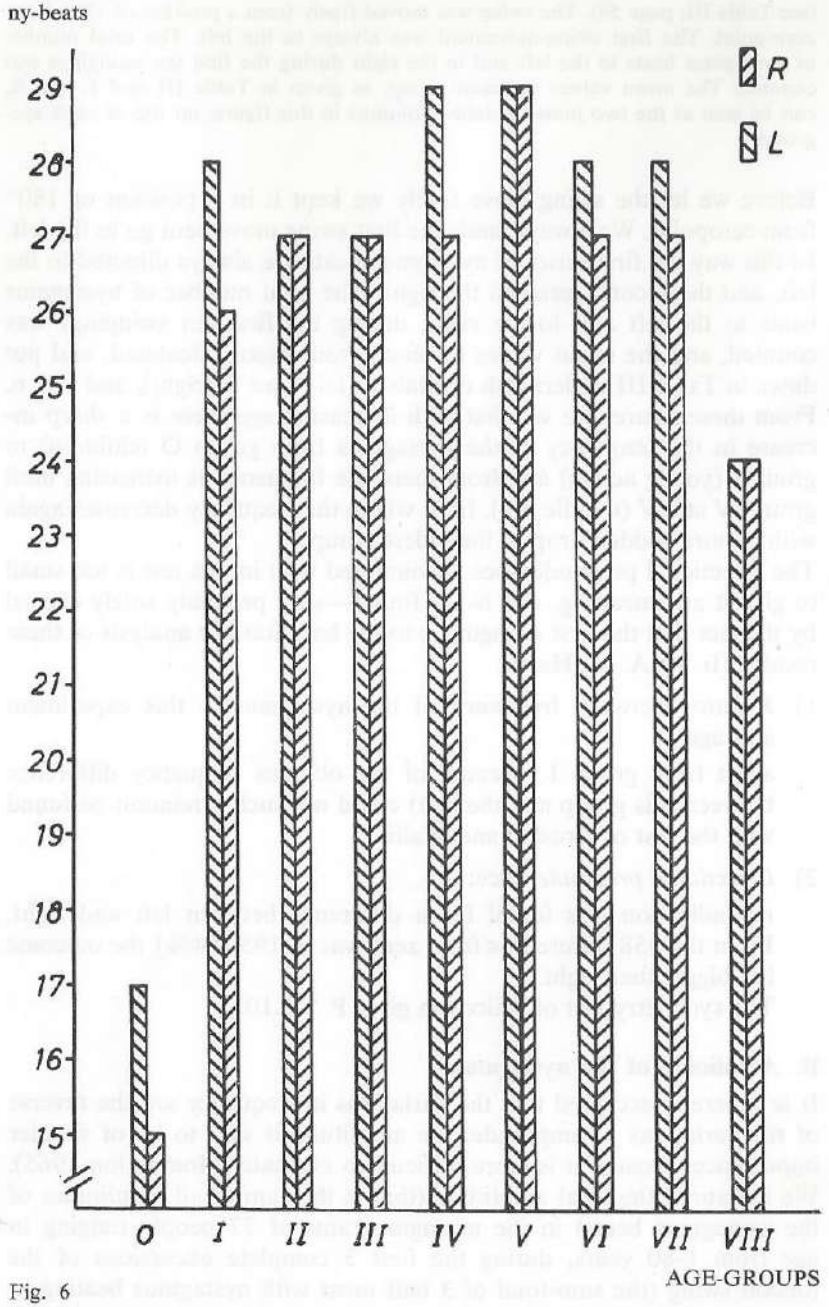


Fig. 6

Frequency of the nystagmus and age.

Age-related changes in frequency of the nystagmus measured on a torsion swing,

in a group of 395 subjects from 2–90 years old, subdivided into nine groups (see Table III, page 58). The swing was moved freely from a position of 180° from zero-point. The first swing-movement was always to the left. The total number of nystagmus beats to the left and to the right during the first ten swingings was counted. The mean values for each group, as given in Table III und L and R, can be seen as the two joined hatched columns in this figure, on top of each age-group.

Before we let the swing move freely we kept it in a position of 180° from zeropoint. We always made the first swing movement go to the left. In this way the first series of nystagmus beats are always directed to the left, and the second series to the right. The total number of nystagmus beats to the left and to the right, during the first ten swingings was counted, and the mean values for each group were calculated, and put down in Table III underneath capitals L (left) and R (right), and Fig. 6. From these figures we see that with increasing age there is a sharp increase in the frequency of the nystagmus from group O (children) to group I (young adults) and from there the frequency is increasing until group IV and V (middle age), from where the frequency decreases again with a more sudden drop in the oldest group.
The directional preponderance encountered with in this test is too small to give it any meaning, and is—if found—very probably solely caused by the fact that the first swinging is to the left. Statistic analysis of these results. (Ir. A. A. M. Hart).

1) *Relation* between **frequency** of the nystagmus in this experiment and **age**:
   apart from group I (because of the obvious frequency difference between this group and the rest) could not such a relation be found with the test of Kruskal and Wallis.
2) *Directional preponderance*:
   no indication was found for a difference between left and right. From the 358 differences from zero was in 195 (54%) the outcome left bigger than right.
   The symmetry test of Wilcoxon gives $P > 0.10$.

B. Amplitude of the nystagmus

It is generally accepted that the variations in frequency are the reverse of the variations in amplitude; the amplitude is said to be of smaller importance, because it is more difficult to evaluate (Montandon 1965). We measured the total amplitude (that is the sum of all amplitudes of the nystagmus beats) in the nystagmograms of 77 people ranging in age from 1-80 years, during the first 3 complete excursions of the torsion swing (the sum-total of 3 half turns with nystagmus beating to the left and of 3 half turns with nystagmus beating to the right). We tried to keep the duration of the periods at 20 seconds, and added or

took away weights underneath the chair in order to obtain this result (see before).
All our subjects conformed to our criteria and were examined with the usual precautions.
Table IV gives the subdivision of the 77 subjects into 8 groups according to their ages. The total value of the amplitude is given for each semi-turn, starting with T 1 as the first semi-turn to the left with nystagmus beating to the left, and T 6 the last semi-turn of the 3d excursion. This was done by measuring the amplitude of each simple nystagmus beat in millimeters from the base line, for each semi-turn, for every individual test-subject and adding these small values together. These values, for each semi-turn were added together for the subjects belonging to the same age-group. The mean total amplitude in each group for every semi-turn is also given. At the end, the total amplitude for all groups calculated for every semi-turn (T) with their mean value, is given.
The mean values of T1-T6 for each group are graphically laid down in Fig. 7, which shows that the highest values for the amplitude are reached in the youngest age group (1-10 years), high values in the teen-age group (11-20 years), from here we see the values gradually getting smaller, until the age-group VI (51-60) whereafter increase of the value is noticed.

TABLE IV
Total and mean values of the sum of the individual amplitudes in age-groups.

Age-group		T 1	T 2	T 3	T 4	T 5	T 6
I	1–10	130.2	146.8	123.9	122.5	117.1	129.7
: 12		10.8	12.2	10.3	10.2	9.8	10.8
II	11–20	115.9	109.2	116.7	105.5	97.6	103.4
: 13		8.8	8.4	9.0	8.1	7.5	8.0
III	21–30	77.5	76.0	70.9	75.8	71.7	66.4
: 12		6.5	6.3	5.9	6.3	6.0	5.5
IV	31–40	22.2	24.4	18.8	22.0	20.7	18.4
: 4		5.6	6.1	4.7	5.5	5.2	4.6
V	41–50	42.6	48.7	46.1	50.4	42.8	37.9
: 9		4.7	5.4	5.1	5.6	4.8	4.2
VI	51–60	14.4	13.3	12.8	14.7	15.4	12.2
: 4		3.8	3.5	3.2	5.1	4.5	4.1
VII	61–70	35.1	40.6	47.5	35.5	42.1	32.6
: 10		3.5	4.1	4.8	3.6	4.3	3.3
VIII	71–80	55.8	58.2	57.9	54.8	47.8	49.2
: 13		4.3	4.5	4.5	4.2	3.7	3.8
T		531.3	524.0	497.2	492.9	460.6	461.8
: 77		6.9	6.8	6.5	6.4	6.0	6.0

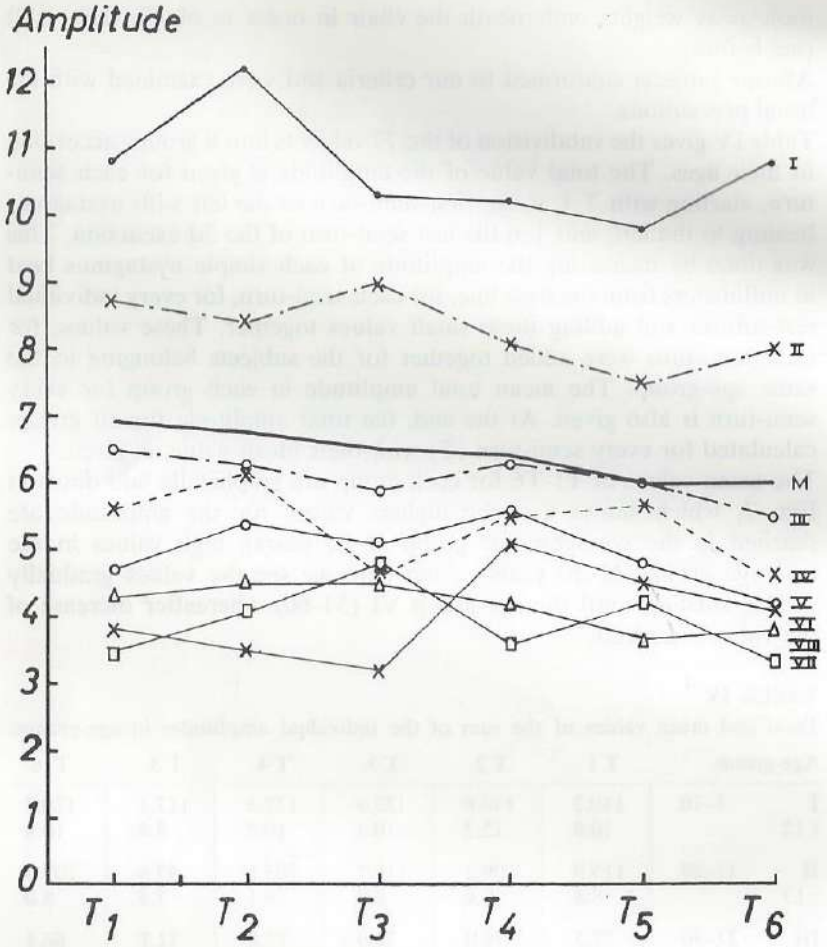


Fig. 7

Amplitude of the nystagmus and age.

Variations in the total amplitude of nystagmus with increasing age in 77 subjects between 1–80 years old (see Table IV, page 61) subdivided into eight groups (I, II, III, etc.) measured on a torsion swing during the first three excursions i.e. 6 half turns (T1–T6). The mean total amplitude in each group for every semi-turn is given (Table IV).

M is the mean of the total amplitudes for all groups together.

Amplitude is given in mm.

C. The slow phase of the nystagmus

Most authors agree that the slow phase of the nystagmus is of vestibular origin (Buys 1924; Dohlman 1936; Hendriksson 1955). The slow component of the nystagmus is produced by impulses via fibres ascending in the medial longitudinal fasciculus and the reticular formation,

to the eye-muscle nuclei (Szentagothai 1950). Slow component fibres send branches to high threshold reticular-activating neurons which, when their threshold is reached, fire and produce the quick phase. As this neuron fires, it fires upon a reticular inhibitor-neuron which acts to cut of the flow of incoming slow component discharges. The first nystagmic cycle is thus born (Brodal et al. 1957, 1962; Carpenter 1960, 1966).

According to Fluur (1962) there are two centres where the slow movement of the nystagmus can be elicited:

1. In the nucleus interstitialis of Cajal for vertical and rotatory movements and
2. in the mesencephalic reticular formation for horizontal movements.

These two centres apparently function quite independently of each other, as evidenced by both clinical and experimental investigations (Breinin and Moldaver 1955; Moldaver and Breinin 1956; Fluur 1959).

The most characteristic quantitative criterium of the slow phase is its slope, whose angle is in proportion with the size of the stimulus. In the torsion-swing test according to Greiner et al. (1968), the slow phase is in direct proportion with the value of the maximum acceleration. So the slow phase seems to express very well the sensitivity of the vestibular apparatus. Maspetiol and Keravec (1962) determined the product

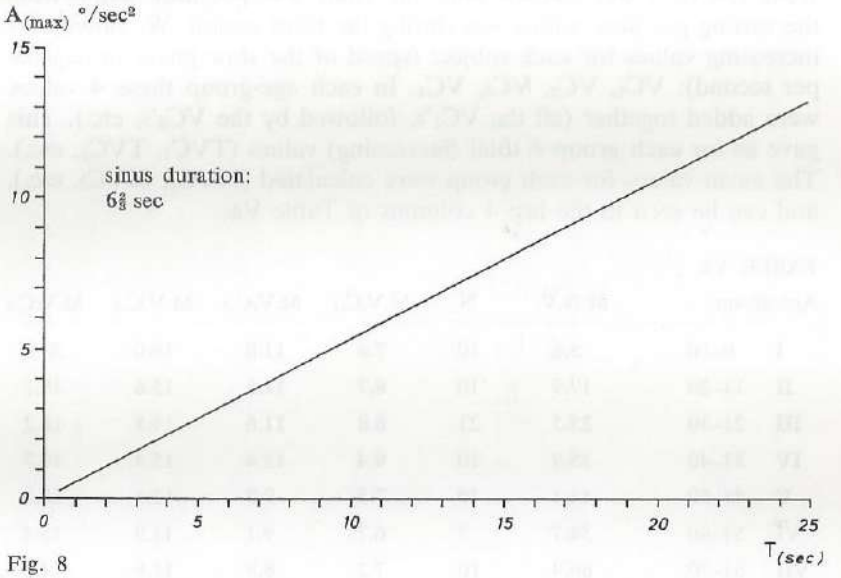


Fig. 8

Linear increase of the angular acceleration on a mechanically driven torsion swing (Fig. 15). The fixed time of each oscillation-period is 6⅔ sec. The linear increase of the angular acceleration $A_{(max)}$ in °/sec² as a function of time can be read in this figure up to 25 seconds.

correlation between the different quantitative parameters and came to the conclusion that the maximum speed of the slow phase was the best parameter for measuring the vestibular reaction quantitatively.

The possibility of an age-dependency of the slow phase of the nystagmus was studied in the following experiment on the torsion swing. A mechanically driven rotational chair (Fig. 15) was used which could produce a sinusoidal movement. The fixed time of each oscillation period was $6\frac{2}{3}$ sec. We started from the resting position so that a slowly increasing angular acceleration was obtained. The linear increase of the angular acceleration as a function of the time can be (up to 25 seconds) read in Fig. 8. A nystagmic response appeared when the stimulus was strong enough, and this nystagmus was recorded. We made thus recordings of 113 people between 2 and 91 years old, subdivided into 10 groups according to their ages. The mean age value (M.A.V.) is given for each group, and also the number of individuals in each group (N) (Table Va, first 3 columns).

These test-subjects conformed to our criteria. The test was performed according to our previous described standards.

In order to obtain comparable values, the speed of the slow phase in each individual subject was measured at the same time of the second half of each period (during 4 successive periods), so always with the nystagmus beating in the same direction. The first measuring was done from $13\frac{1}{3}$ ($2 \times 6\frac{2}{3}$) seconds after the chair was put into action from the resting position, which was during the third period. We now got 4 increasing values for each subject (speed of the slow phase in degrees per second): VC_1, VC_2, VC_3, VC_4. In each age-group these 4 values were added together (all the VC_1's, followed by the VC_2's, etc.). This gave us for each group 4 total (increasing) values (TVC_1, TVC_2, etc.). The mean values for each group were calculated (MVC_1, MVC_2, etc.), and can be seen in the last 4 columns of Table Va.

TABLE Va

Age-group		M.A.V.	N	M.V.C.1	M.V.C.2	M.V.C.3	M.V.C.4
I	0–10	5.6	10	7.6	11.8	16.0	24.0
II	11–20	17.9	10	8.7	11.8	15.6	19.1
III	21–30	25.5	21	8.8	11.6	14.5	18.2
IV	31–40	35.9	10	9.4	13.4	15.4	19.7
V	41–50	44.1	10	7.5	9.8	12.9	18.0
VI	51–60	54.7	7	6.7	9.1	11.9	15.4
VII	61–70	66.4	10	7.2	8.9	11.9	14.1
VIII	71–80	75.7	20	9.7	11.8	13.3	15.6
IX	81–90	83.2	13	9.7	11.2	13.3	14.7
X	>90	91.0	2	7.5	10.5	13.0	16.5

TABLE Vb

see Fig. 9

Age-group		M.A.V.	N	M.V.C.1	M.V.C.2	M.V.C.3	M.V.C.4
I	0–10	5.6	10	10	15.5	21.1	31.6
II	11–20	17.9	10	10	13.6	17.9	21.9
III	21–30	25.5	21	10	13.2	16.5	20.7
IV	31–40	35.9	10	10	14.3	16.4	21.0
V	41–50	44.1	10	10	13.1	17.2	24.0
VI	51–60	54.7	7	10	13.6	17.8	23.0
VII	61–70	66.4	10	10	12.4	16.5	19.6
VIII	71–80	75.7	20	10	12.2	13.7	16.1
IX	81–90	83.2	13	10	11.5	13.7	15.2
X	> 90	91.0	2	10	14.0	17.3	22.0

In order to arrange the course of the slow phase during this increasing stimulation on the torsion swing more conveniently, we took the value 10 (in degrees per second) as a basic value for all the MVC_1's, and from this value — by means of a simple multiplication — the other three values were converted accordingly. The outcome is seen in the last 4 columns of Table Vb, and a good survey of these results is seen in Fig. 9. We notice a very good vestibular reaction in group I. For the next three groups the values are lower, more or less the same, increasing up to group IV. From here there is a slowing down of the reaction with a tendency in the higher age-groups to increase again.

Because there were only two people over 91, we omitted group X from Fig. 9.

D. The quick phase of the nystagmus

We use the definition of nystagmus according to Janeke (1968) i.e. a rhythmical eye movement characterized by a fast and a slow phase. The relationship between the slow and the quick phase is up to the present day still unsettled. The slow phase and its origin have been discussed before.

The question as to which centre is responsible for the fast phase has not yet been answered. There have been discussions for many years and we give a survey of these theories on the following pages.

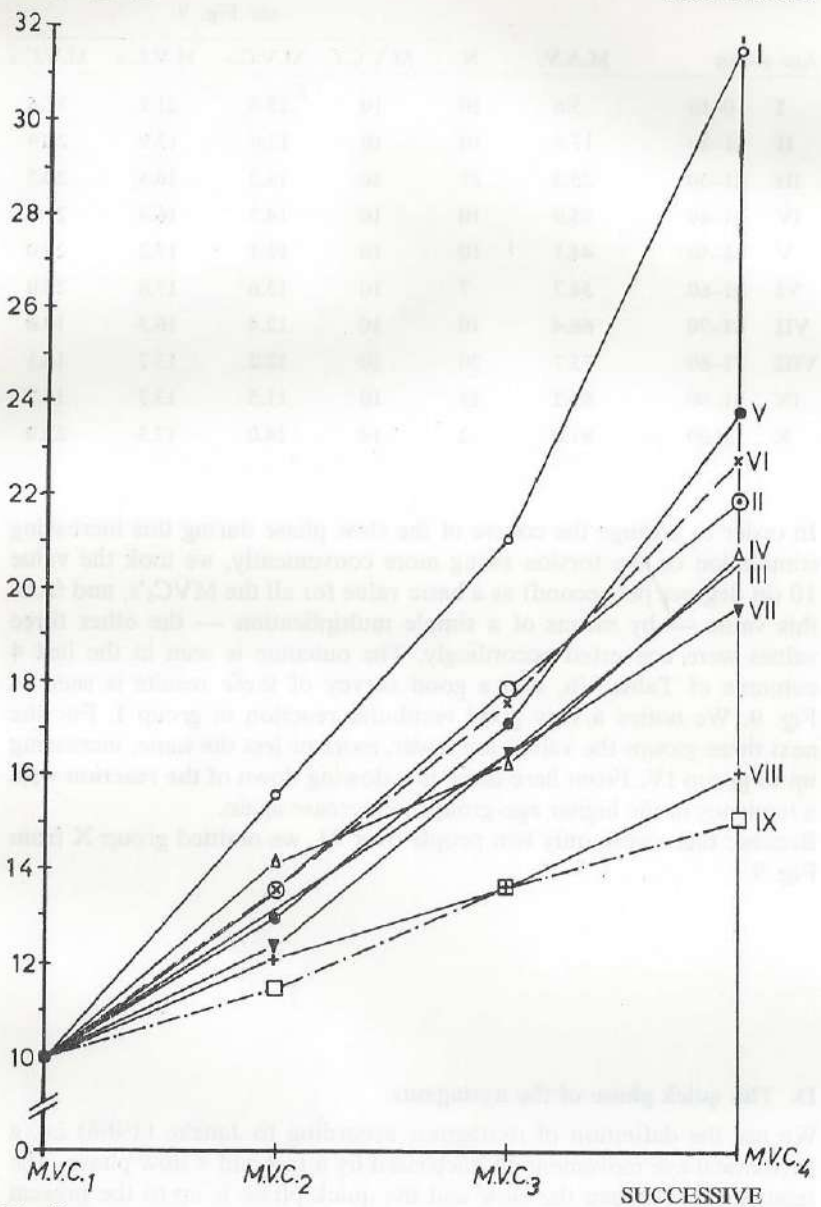


Fig. 9

The slow phase of nystagmus and age (see Table Vb last four columns, page 65). The course of the slow phase of the nystagmus measured in 113 subjects between 2–91 years old, with increasing stimulation on a torsion swing. MVC_1, MVC_2, MVC_3, and MVC_4 are the mean values (for each age-group) of the speed of the slow phase measured during 4 successive periods.

I. *Cerebral theory of the fast phase of vestibular nystagmus.*

II. *Origin in parts of the vestibulo-ocular reflex arch.*

ad. I.

Mahoney et al. (1957) believed the origin of the fast phase to be in the cortex. Bartels (1910) held already a cortical theory and Rosenfeld (1911) was of the opinion that in the frontal lobe there existed a cortical centre for the rapid phase. But it is well-known that nystagmus can be induced even in decerebrated animals and an-encephalic babies.

ad. II.

1. *Proprioceptor theory* assumes that the rhythmic reaction is due to proprioceptive impulses from the ocular muscles. Tozer and Sherrington (1910) found proprioceptive nerve-endings in the eye muscles and Bartels (1914); Gabersek and Jobert (1965) thought the beginning of the reflex arch for the quick phase to originate here. This theory is refuted by the normal production of nystagmus when the proprioceptors have been paralysed by the injection of procaine hydrochloride into the ocular muscles (De Kleyn 1922).

2. *The ocular-muscle nuclei theory* which locates the origin of the rhythm in the nuclei of the motor nerves to the ocular muscles. The assumption is that there exists a mutual inhibition of the oculomotor nuclei. Wendt (1951) and Fluur (1962) placed the origin of the fast phase at the level of the oculomotor nuclei. This theory is made improbable by the failure, when only one oculomotor nucleus remains connected with the vestibular nuclei, of the internal rectus muscle innervated by the opposite third nucleus to contract rhythmically on labyrinthine stimulation (Spiegel 1929). This shows that the mutual connections of the two oculomotor nuclei are unable to produce the rhythm.

3. *The labyrinthine theory* which seeks the origin of the rhythm in the labyrinth. Rejtö (1920) thought that the reaction was produced from the maculae. This theory is refuted by the failure of elimination of both labyrinths to prevent nystagmus of central origin (Bechterew's compensatory nystagmus) or nystagmus following punctures of the vestibular nuclei (Spiegel and Sato 1926).

4. *The vestibular nuclei theory* which attempts to localize the origin of the rhythm in the vestibular nuclei. This theory was held by Bauer and Leidler (1912); Spiegel and Sato (1927); Ohm (1914, 1916, 1939, 1940); and Spiegel and Price (1939).

5. *The reticular-substance theory* which localizes the origin of the rhythm in the substantia reticularis. This theory was held by Lorente de Nó (1933); Mittermaier (1952) and was refuted by Spiegel and Price (1939). Duensing and Schaeffer (1957) found units in the reticular formation which discharge synchronously with the quick component and units synchronous with the slow component. Similar units were also

found in the medial longitudinal fasciculus that receives its fibres from the vestibular nuclei. An interaction between some units of the vestibular nuclei and the reticular formation was demonstrated.
Nowadays the problem seems to be restricted to the alternative between the vestibular-nuclei theory and the reticular substance theory.
Lachmann, Bergmann, and Monnier (1958) described a meso-diencephalic nystagmogenic area in rabbits. Oosterveld (1963) and Montandon (1964) found that by simultaneous stimulation of this area and the labyrinth, subtraction or summation phenomena appear. In 1964 Gernandt showed that stimulation of the vestibular nerve elicits unit discharges in the reticular formation that are more complex than those recorded from the vestibular nuclei. Following Gernandt's findings, Spiegel (1964) ceased to refute that the reticular formation plays a part in the genesis of the fast component.
Kornhuber (1966) believes that the generative mechanism of the fast phase which is influenced by the cortex is formed by the premotor apparatus of the oculomotor nuclei, i.e. the gaze centres of the para-median reticular formation situated in the pons and the midbrain.
The reticular formation theory is considered more and more acceptable, but the existence of all these hypotheses indicates the complexity of the origin of the fast phase and the obscurity of its real origin (Biemond 1961).

Extra-vestibular influences on vestibular reactions.

1. The level of alertness, fatigue, and cerebral excitation.

The sensitivity of the system generating the quick phase of nystagmus to changes in the level of alertness is known from the studies of Collins (1962); Collins and Guedry (1962); and Crampton and Schwam (1961). With excitation the experimental nystagmus increases, during sleep and anaesthesia the nystagmus disappears. Fluctuations in the cerebral excitation that will influence the nystagmus do not necessarily have to show in the E.E.G. (Kornhuber 1966). The nystagmus and particularly the quick phase is one of the most sensitive indicators of fatigue. Fatigue gives a slowing down of the quick phase and pauses develop (Megighian and Waldecker 1961). During caloric tests Clement (1970) noticed the occurrence of pauses in all subjects. They were more frequent during the culmination period, but their duration increased proportionally to the decrease in speed of the slow phase. With the arousal technique the number of pauses remained but there was a significant decrease in the duration of the pauses. He tried to explain "attention" on a neuro-physiological base. From the literature he deduced that alertness goes together with "facilitation" of the stimulus-conduction, and also together with a raised nystagmus threshold. He also pointed out that certain eye-movements give more information on the decreasing degree of alertness before falling asleep than does the E.E.G.

2. Habituation (see before).

During the development of habituation there is an increase in the rate of the quick phases of nystagmus in spite of a decrease in the velocity of the slow phase (Collins 1964). According to this author, the base of the vestibular habituation lies in the medulla, most probably in the nuclei vestibulares and their connections with the bulbopontine reticular formation and the cerebellum.

3. Fixation and light and darkness.

Visual fixation gives a suppression of both slow and fast phases of the vestibular nystagmus.

4. Respiration.

There are narrow connections from the vestibular part of the reticular formation of the medulla to the respiration centre. Suppression of the respiration gives an inhibition of the vestibular nystagmus. Also in the period before falling asleep (see before) the efficiency of the lung function decreases from 75% to 54% (if 100% is the total lung capacity, and 75% the normal working capacity).

5. Age.

Increasing age plays a part in the here-mentioned factors. The vital capacity of the lungs — because of senile emphysema — decreases from 75% to 44% (Bates and Christie 1955). So we can expect an inhibition of the vestibular nystagmus in the older patient, and a "facilitation" in the young person.

The quick phase of the nystagmus.

The course of the quick phase of the nystagmus was followed during a linearly damped sinusoidal stimulation lasting 2 minutes in a group of 72 test subjects of different ages in order to study whether any differences existed in the decline of the quick phase with decreasing stimulation, for the different age groups with increasing age. The test subjects varied in age between 2 and 80 years and were subdivided according to their age into 8 groups:

Group	I	Age	1-10 years
	II		11-20 „
	III		21-30 „
	IV		31-40 „
	V		41-50 „
	VI		51-60 „
	VII		61-70 „
	VIII		71-80 „

They all had to conform to our standards.
About the examination technique, recording of the nystagmus and calibration, see under "torsion swing".

TABLE VI

Age-group	Number	Observations						Decrease %
		T 1	T 2	T 3	T 4	T 5	T 6	
I	10	800	795	786	785	775	771	
II	9	656	641	631	619	608	591	
III	14	1037	1023	997	973	945	922	
IV	5	360	354	340	335	324	311	
V	10	676	663	647	633	621	601	
VI	3	188	184	177	173	170	160	
VII	9	594	584	564	549	536	515	
VIII	12	855	834	806	789	763	735	
Total	72	5166	5078	4948	4856	4742	4606	
Mean %		100	98.3	95.8	93.9	91.8	89.2	10.8

The duration of each period was 20 seconds, the time constant used was 5 seconds and the paper speed rather quick, 25 mm/sec, in order to make it easier to calculate the speed of the quick phase, this was done by measuring the degrees of the angle, the slope of the quick phase makes with the horizontal. This was done by making 6 observations (T1-T6) during 6 successive periods, each at the same moment after the start of the period concerned, where the amplitude of the torsion swing was 90° and the angular acceleration 9°/sec² (see before: torsion swing, duration of the period). The test was started by giving the torsion swing a maximum excursion of 180° to the right, so that the first swinging was to the left. We let the swing complete six excursions.

The natural decline of the excursions of the torsion swing because of the damping, is seen in Fig. 10, and the mean value, in %, of the speed of the quick phase (of 72 test subjects during 6 successive observations) is seen in Fig. 11 from which is learned that there is a linear decrease in the speed of the quick phase with increasing age, in accordance with the decrease of the stimulation. The mean values are given in Table VI at the bottom where for each age-group the total of individual values for the first observation are given under T 1, the total of the individual values for the second observation under T 2 etc.

In Table VII the age groups are given as in the former table, but now the total of the individual values under T 1 are reduced to a uniform value of 100, and the following figures under T2—T6 were adapted to

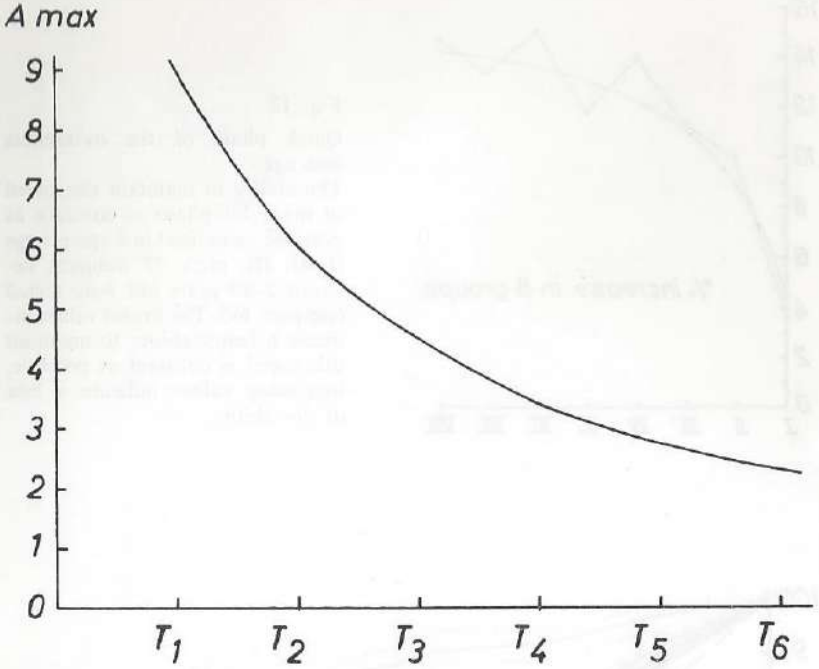


Fig. 10

Natural decline of the excursions of a torsion swing because of the damping, as a function of time (O — T_1 = 20 seconds, T_1 — T_2 = 20 seconds, O — T_6 = 120 seconds). A max is the maximum angular acceleration at the beginning of each period (see page 70).

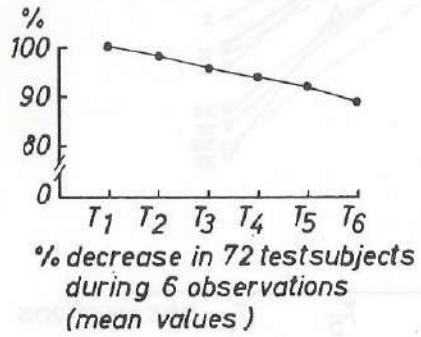


Fig. 11

(See Table VI basal column, page 70). The decrease (in percentage) of the mean value of the quick phase of nystagmus measured in the total of 72 test subjects between 2 and 80 years old, on a torsion swing during six excursions.

this first value, which gives us the decrease in the speed of the quick phase for each age-group in percentage, the last column giving the total decrease for each group in percentage. These last figures are laid down in Fig. 12. Here it can be seen that the ability for maintaining the speed of the quick phase as constant as possible is the best in the youngest group (the decrease here is only 3.6%) and with increasing

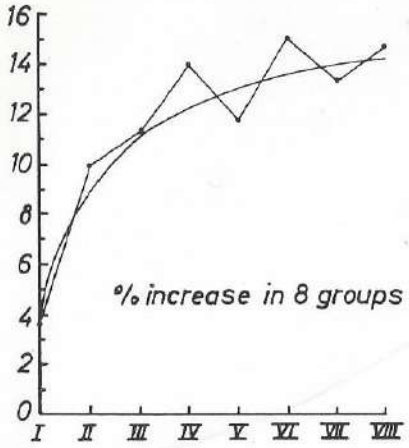


Fig. 12
Quick phase of the nystagmus and age.
The ability to maintain the speed of the quick phase as constant as possible, visualized in 8 age-groups (I, II, III, etc.). 72 Subjects between 2–80 years old were tested (see page 69). The lowest values indicate a better ability to maintain this speed as constant as possible, increasing values indicate a loss of this ability.

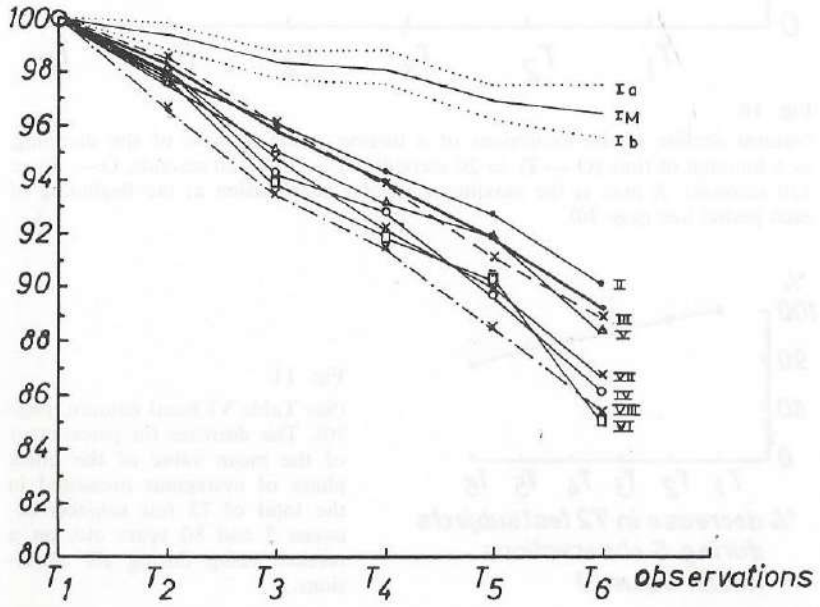


Fig. 13
Quick phase of the nystagmus and age.
Decrease of the speed of the quick phase of nystagmus in 72 subjects between 2–80 years old, subdivided into eight groups (I–VIII, see page 69). For each group this decrease is measured during 6 successive periods on a torsion swing (see Table VII).
Group I is subdivided into group Ia (2–5 years old) and group Ib (6–10 years old).

age this loss slowly increases, coming to the highest value of 15.0 in the 51-60 group, where after we found slightly lower values).
In what way each group contributes to this steady decrease in speed of the quick phase is seen in Fig. 13 which is derived from Table VII, but with an additional subdivision of group I.
Group Ia consists of 5 children between 2 and 5 years, and Group Ib of 5 children between 6 and 10 years old.

TABLE VII

Age-group	Number	Observations						Decrease %
		T 1	T 2	T 3	T 4	T 5	T 6	
I	10	100	99.4	98.3	98.1	96.9	96.4	3.6
II	9	100	97.7	96.1	94.3	92.7	90.1	9.9
III	14	100	98.6	96.1	93.8	91.1	88.9	11.1
IV	5	100	98.0	94.2	92.8	89.7	86.1	13.9
V	10	100	97.5	95.1	93.1	91.8	88.3	11.7
VI	3	100	97.7	93.9	91.9	90.3	85.0	15.0
VII	9	100	98.1	94.8	92.2	90.0	86.7	13.3
VIII	12	100	96.7	93.5	91.5	88.5	85.3	14.7

From this Table and Fig. 13 (Ia + b) is shown that the very young have the greatest ability in keeping the quick phase more or less constant, the total decrease in % is only 2.5.
The mean values of decrease in the total of 72 test subjects for the 6 successive observations (Fig. 11) are also put in Fig. 13, so that can be seen clearly how each group contributes to the decrease of the speed of the quick phase with increasing age.

E. The threshold of the nystagmus for rotatory stimulation of the horizontal semicircular canals

For a long time physiologists have been trying to establish the threshold of the semicircular canals for rotatory stimulation (Jongkees 1969). It became clear that the vestibular receptors are, in susceptibility and precision, the front-ranking sense-organs in human beings and animals (Trincker 1960, 1961). The definition of the threshold always depends on the method used, and by using more refined techniques it is always possible to find a lower threshold.
It is important to know the sensitivity of the muscle reactions (like for instance of the nystagmus) to be measured. For the nystagmus the

threshold of the quick phase is higher than the threshold of the slow component. Measurements on the rotational chair give different results from those obtained with sinusoidal stimulation on the torsion swing.
With the same methods, higher values are found in old people than in younger age groups (Groen and Jongkees 1948). According to Mulder's law the size of a stimulus must be expressed as $\alpha \; t = s_{minimal}$. The threshold should not be described as an acceleration, but as an "impulse" $s_{minimal}$ = acceleration times duration.
α = angular acceleration in °/sec², t = time in seconds.
Van Eyck et al. (1957) could detect obvious muscle reactions (neck muscle reactions) in pigeons at s = 1,5°/sec. Ek et al. (1960) could still detect the influence of stimulations of s = 0.04°/sec on head movements of pigeons. Oosterveld et al. (1969, 1970) described oculogyral illusions observed in aircrew of a jet aircraft and found that the threshold value of the horizontal semicircular canals for angular accelerations also depends on gravity. Other factors that define the value of the vestibular threshold are drugs, like alcohol, even alcohol taken up to 24 hours before. The lowest value measured during these experiments was 0.036°/sec. The subjective sensation threshold seems to be of small or no clinical value (Van Eyck, Jongkees, and Klijn 1957).
According to Montandon et al. (1969) the threshold of the nystagmus is a frequency threshold. It corresponds to the lowest grade of intensity of a continuous and constant stimulation that is able to provoke and maintain until the end of the stimulation period a nystagmic reaction of a definite direction and of one beat per second. The nystagmic reaction is a rhythmic process (Monnier 1967) of diphasic beats with a slow and a rapid phase which occurs in three stages: latency time, start of response, and a period of state (maximum) frequency. Only the last period of a maximum frequency must be taken into consideration for the determination of the threshold. The two preceding periods, possibly reaching 10 to 20 seconds are not suitable for a quantification. A minimum duration of 20 to 30 seconds of stimulation at a constant intensity is consequently required. Other parameters like amplitude or speed of the slow phase are not considered. The main parameter for the nystagmic threshold is a frequency threshold and the recording has to be carried out in complete darkness.
Montandon (1965) also used a damped sinusoidal stimulation (torsion swing) to determine the nystagmic threshold: the value of the angular acceleration where the nystagmic response stops. This is the "descending threshold" because the stimulus is a decreasing one. On the other hand when the stimulus should be increasing an "ascending threshold" is found. The latter is mostly slightly lower (Greiner et al. 1967). It is more difficult to find the descending threshold, because of the time involved; if it should last more than 5 minutes all kinds of irregular

eye-movements are encountered with, since habituation and pattern activity interfere.
The threshold found with a damped sinusoidal stimulation is always higher than with other techniques, because the test subject is not submitted to a constant acceleration, and the preliminary acceleration is only applied for a very short period (Greiner et al. 1966).

Threshold value change with increasing age, expressed in Latency

We examined a group of 122 people on the torsion swing with ages ranging from a few days till 94 years. According to their age they were subdivided into 11 groups (Fig. 14 and Table VIII).
A mechanically driven rotational chair (Fig. 15) was used which with a fixed period of $6\frac{2}{3}$ sec could produce a sinusoidal movement with a slowly increasing angular acceleration and deceleration. With this slowly increasing sinusoidal stimulation a nystagmic response was recorded after a certain time and this time-value was found to vary for people belonging to different age-groups. The threshold value of the

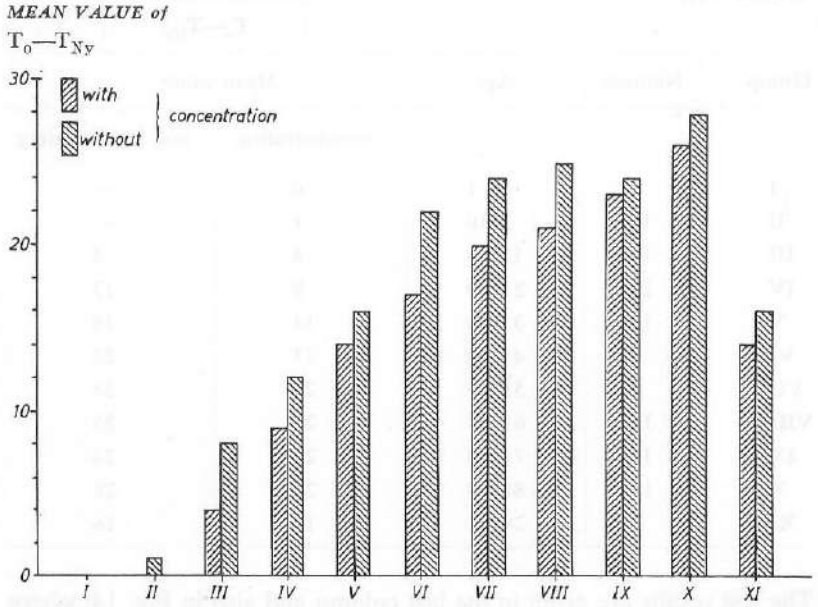


Fig. 14
The latency of the nystagmus with increasing age.
The time-gap (T_0—T_{Ny}) before recording the quick phase of nystagmus with increasing stimulation on a torsion swing, in 11 age-groups: I, II, III, etc. (122 subjects between 0—94 years old) (see Table VIII, page 76). From group 2 onwards we got 2 values: with concentration (while the test-subject was doing mental calculations) and without concentration (while he was relaxing); this is shown in the 2 joined hatched columns.

nystagmus can now be found with the formula $s = \alpha t$ where t is the time during which the stimulation was applied and α is the maximal angular acceleration during that time, and can be found in Fig. 8, where can be seen that with a sinus-duration of $6\frac{2}{3}$ sec, there is a linear and rather steep increase of the maximal angular acceleration. The values (s) which are "threshold values" for this special experiment, were not used, but we compared, in this group, the T_o-T_{Ny} values. T_o is the time where the movement of the chair was put into action and T_{Ny} the time where the first nystagmus response is recorded, so actually T_o-T_{Ny} can be called the Latency. As usual it was impossible to detect the beginning of the slow phase of the very first nystagmus beat so the first quick phase was taken as the beginning of the reaction. For each subject this T_o—T_{Ny} value was established, firstly (c), while the patient was concentrating, secondly (n.c.), while he was relaxed. The total of these values for the people belonging to one group was taken, the mean value was calculated and put down in Table VIII.

TABLE VIII

			T_o—T_{Ny}	
Group	Number	Age	Mean value	
			concentrating	not concentrating
I	9	0– 1	0	—
II	11	2–10	1	—
III	10	11–20	4	8
IV	21	21–30	9	12
V	11	31–40	14	16
VI	8	41–50	17	22
VII	8	51–60	21	24
VIII	11	61–70	21	25
IX	19	71–80	23	24
X	12	81–90	26	28
XI	2	> 91	14	16

The test results are given in the last column and also in Fig. 14, where on the abciss the age groups and on the ordinate the time value T_o-T_{Ny} can be seen.
The first value in the last column (from group III onwards) corresponding to the shorter column on the abciss of Fig. 14, is the value obtained while the patient concentrated, the second value corresponding to the second — and longer — column on the abciss was obtained while he was relaxed. Group I, a group of young infants, ranging

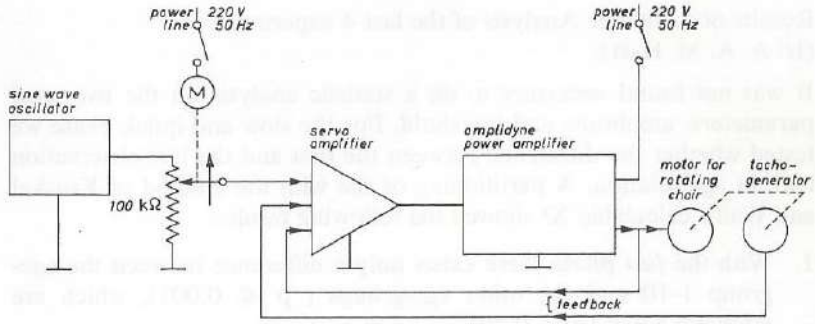


Fig. 15
Block diagram of the electrical arrangements of the mechanically-driven torsion swing.

from 1-7 days old was kept in an alert state on the lap of the nurse who was sitting on the torsion-swing chair.
Group II, a group of young children were kept busy by asking them simple questions that had to be answered, partly to reassure them, because the test was performed in complete darkness and at the same time to keep them alert. We omitted the second round "not concentrating" because the small children got frightened when we let them sit for five minutes in the dark, and so we did not achieve our purpose to let them relax.
In general, test-conditions were as mentioned in the previous experiments.

Calibration, recording (see before).

The test was, from group III onwards done in two stages:

a. while the patient was doing mental calculations,

b. while he was relaxing.

Between these two stages we allowed a time of 5 minutes, during which period the subject was sitting in complete darkness.
For group I it was impossible to put down exactly the T_{Ny}, because in most of the babies we saw immediately after the chair was put into action (T_o-T_{Ny}) a nystagmus. These babies were healthy new-borns ranging from 1-7 days old. There seems to be no inhibition at all. From the age of 2 years onwards the value T_o-T_{Ny} is growing with increasing age, but after the age of 90 it might be getting smaller again, but this group (group XI) only consisted of two subjects of 94 years old, so too few to give a positive answer.

Results of a Statistic Analysis of the last 4 experiments.
(Ir. A. A. M. Hart).

It was not found necessary to do a statistic analysis on the two used parameters: amplitude and threshold. For the slow and quick phase we tested whether the difference between the first and the last observation had an age relation. A partitioning of the with the method of Kruskal and Wallis calculable X^2 showed the following results:

1. With the *fast phase* there exists only a difference between the age-group 1-10 and the other age-groups ($p \ll 0.001$), which are mutually equal ($p > 0.80$).
2. With the *slow phase*, 3 groups can be distinguished:
   a. the age-group 1-10
   b. the age-group 11-60
   c. the age-group over 60

Testing of the difference between group a and group b gives $p < 0.01$, and of the difference between group b and group c $p \ll 0.001$. Between the age-groups 11-20, 21-30, 31-40, 41-50, and 51-60 no difference was found ($p > 0.80$) and neither between the age-groups 61-70, 71-80 and over 80 ($p > 0.50$).

CHAPTER IV

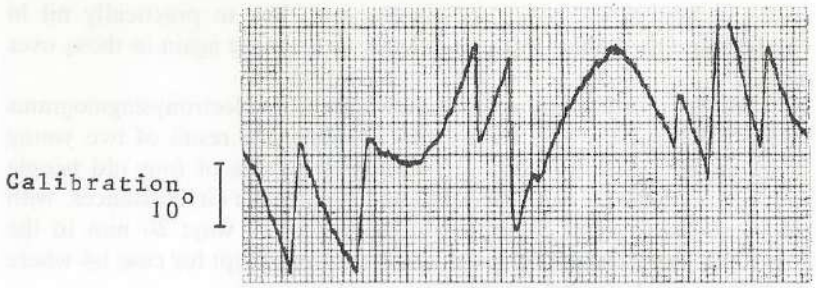
Discussion of the results of own experiments and the importance with reference to clinical nystagmography.
A few examples of nystagmograms are given.
Hearing loss, ataxia, and complaints of vertigo are commonly encountered in old age. These disturbing symptoms, which do not necessarily appear concurrently, may be interpreted as suggesting a degenerative process affecting the entire labyrinth. Although age-related cell loss has been demonstrated in the cochlea long ago, corresponding changes within the vestibular portion could not be found, and only recently it was suggested that presbyacusis and presbyastasis could be the consequences of the same biological process.
The investigation of vestibular function and ageing has been undertaken in a rather small number of studies, and the diversity of methods employed in these studies impairs one's understanding of what changes, if any, may be normally expected as a function of age.
For vestibular nystagmus, the most frequently reported age-effect has been hypo-reactivity, a smaller number of reports have indicated heightened activity with increasing age or no change.
Our own results on age and caloric nystagmus as well as the outcomes obtained with rotationally induced nystagmus will be discussed now.

Regular changes in vestibular responsivity as a function of age were demonstrated with the maximum speed of the slow phase of *caloric nystagmus*.
The means of all four caloric irrigations, with the sequence left cold, right cold, right warm, left warm, were used. The overall trend was that the nystagmic-response strength increased to a maximum at 31—40 years, and declined slowly thereafter. Three possible factors that may well work together are responsible for these changes. Firstly the diminution of vestibular reactions with increasing age, from 41 years onwards, preceded by increasing reactions of the 10—40 years age-group, can be caused by habituation (response increase followed by a response decline, and sometimes in people over ninety, followed again by a response increase) since central inhibitory mechanisms which in some way in adults from 30—40 years onwards, probably by a process of learning, suppress the normal physiological response of the vestibular end-organ. Secondly the assumption is possible that, with increasing age, usually after the age of 50, there is a gradual diminution in blood flow to the labyrinth due to *generalized* athero-sclerosis and to compression of vessels by bony canals as well as to *local* vascular occlusion of labyrinthine vessels as a result of athero-sclerosis of the labyrinth itself.
Thirdly there is degeneration of nervous elements, in the vestibular nerve itself. Clinical implications: comparative clinical examination for vesti-

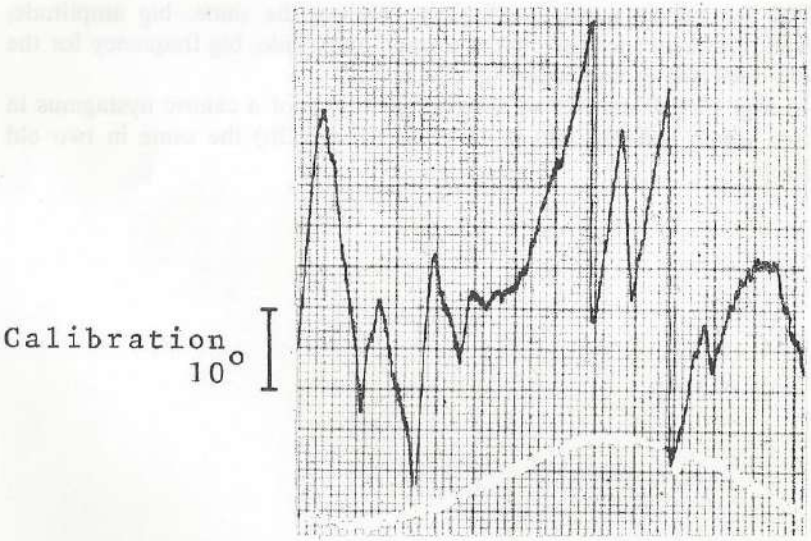
bular function can be done at any age, as long as allowance is made for different reactions in people belonging to different age-groups.
After comparing the results of the caloric response to only cold versus warm stimulation, we can conclude that, additionally, these data reveal a different responsitivity to the warm and cold stimuli in conjunction with age. The older subjects gave a disproportionately greater response to the warm irrigations than to the cold. Also is seen that in the older age-group the warm stimuli tended to elicit a greater response than the cold.
It was further observed that a difference existed in the outcomes of the total caloric reactions (the means of the four values added together) when the sequence cold-warm was used, compared to the warm-cold result. These last results tended to be smaller and mostly so in the young adult groups (21—30, 31—40). The clinical implication of this is that, when doing caloric tests, one should not switch for no reason from a once accepted temperature sequence, otherwise comparison with other tests becomes impossible.

Induced *rotational* nystagmus.
The quantitative elements which can be distinguished in the electronystagmogram obtained during a sinusoidal stimulation are discussed. The *nystagmic frequency*: variations depending on age are shown. The frequency increases sharply from the children's group to the group of young adults. From there a slow increase is seen until the 51—60 year group, whereafter a decrease is seen.
The *amplitude* of the nystagmus follows the frequency in its age-dependency, but it is striking that the amplitude is very pronounced in the very young group. As a whole, the amplitude of the nystagmus seems a very good parameter when we are looking for the age-factor in electronystagmography. The speed of the *slow phase* also follows the age-pattern, showing the best vestibular reaction in the young groups (2—40 years of age) with a decline after the age of 41. When we are looking at, and following the speed of the *quick phase* of the nystagmus with increasing stimulation on a torsion swing in the various age-groups, we discover the same age-patterns as with the other parameters in that the best vestibular reactions are seen in young people (11—40 years old) declining slowly after the age of 41, perhaps the slowest of all parameters employed so far. One could say that the quick phase is the parameter least affected by age-changes, probably because of its origin which is very complex but closely related to the very vital processes of life, like for instance respiration.
From determining the *threshold* of the nystagmus on a torsion swing with increasing stimulation — by establishing the *latency* of the nystagmus — for the different age-groups (this time including a few babies), it was clear that these values also show an age-dependency: the latency

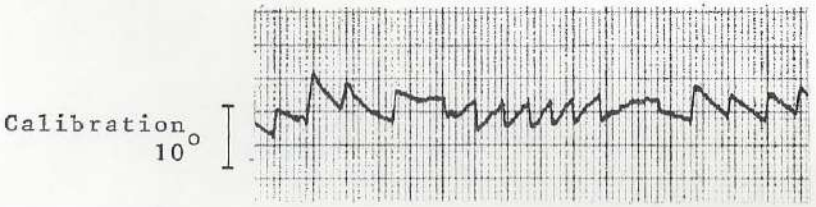
is the highest in the older age-groups, very low to practically nil in children and the babies, with a tendency to decrease again in those over ninety.
To illustrate our findings we give a few cuts from electronystagmograms in Fig.'s 16 and 17. Fig. 16 (a1 and a2) show the result of two young children on a torsion swing, followed by the same of four old people (b1, b2, b3, b4). All were recorded under the same circumstances, with the same mingograph calibrated in the described way; 20 mm in the Fig. is 20°/sec. The paper speed was 1 cm/sec except for case b4 where the paper speed was 2.5 cm/sec.
The most striking in these figures is the big amplitude of the children, compared to the small amplitude of the old people (while the opposite is seen for the frequency).
For the caloric nystagmogram we can say the same: big amplitude, small frequency for the children, small amplitude, big frequency for the old ones (see examples in Fig. 17a and b).
In Fig. 17 (a1 and a2) we see the recordings of a caloric nystagmus in two young children and in Fig. 17 (b1 and 2b) the same in two old people.



a-1) 2 years old.
Nystagmus recorded on a torsion swing during the third period. Paperspeed 1 cm/sec. Time constant 10 sec.

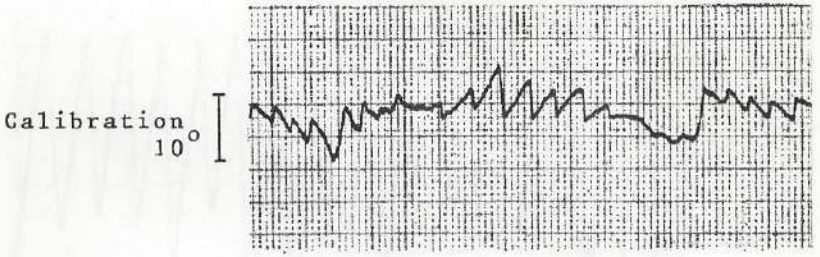


a-2) 2 years old.
Nystagmus recorded on a torsion swing during the third period. Paperspeed 1 cm/sec. Time constant 10 sec.

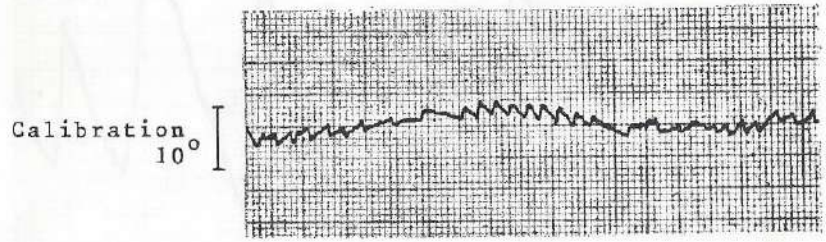


b-1) 76 years old.
Nystagmus recorded on a torsion swing during the third period. Paperspeed 1 cm/sec. Time constant 10 sec.

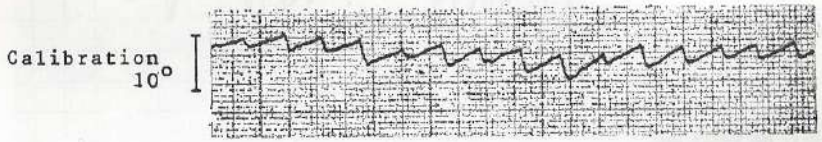
Fig. 16



b-2) 88 years old.
Nystagmus recorded on a torsion swing during the third period. Paperspeed 1 cm/ sec. Time constant 10 sec.

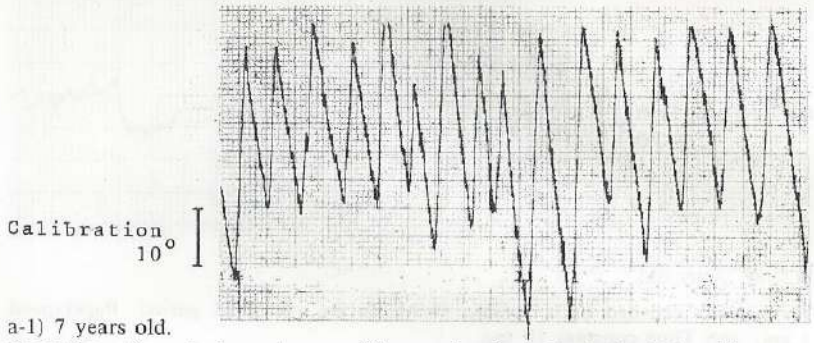


b-3) 79 years old.
Nystagmus recorded on a torsion swing during the third period. Paperspeed 1 cm/ sec. Time constant 10 sec.

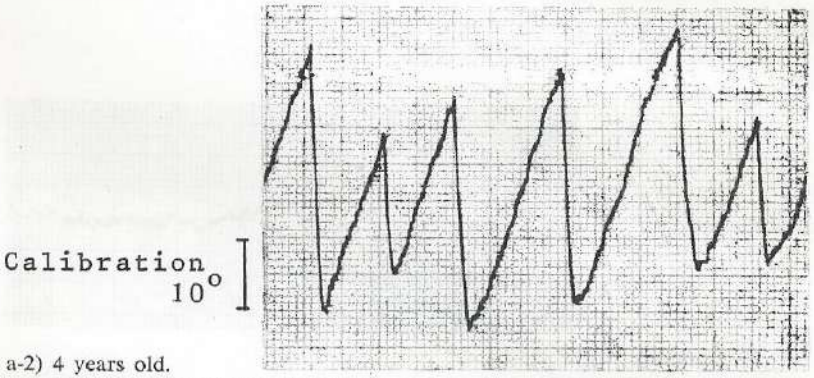


b-4) 71 years old.
Nystagmus recorded on a torsion swing during the third period. Paperspeed 1 cm/ sec. Time constant 10 sec.

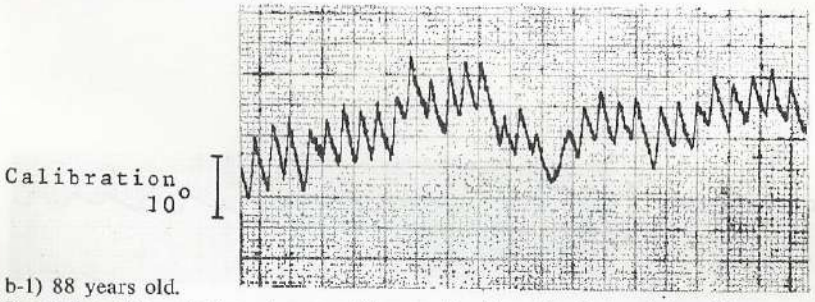
Fig. 16



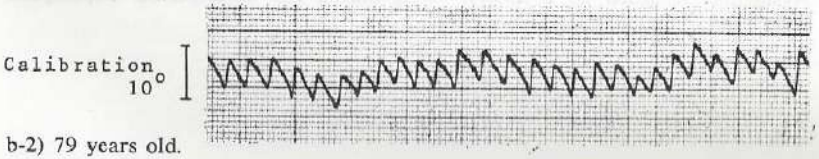
a-1) 7 years old.
Recording of a caloric nystagmus, 30 seconds after stimulation left cold.
Paperspeed 1 cm/sec. Time constant 10 sec.



a-2) 4 years old.
Recording of a caloric nystagmus, 40 seconds after stimulation right cold.
Paperspeed 1 cm/sec. Time constant 10 sec.



b-1) 88 years old.
Recording of a caloric nystagmus, 30 seconds after stimulation left cold.
Paperspeed 1 cm/sec. Time constant 10 sec.



b-2) 79 years old.
Recording of a caloric nystagmus, 25 seconds after stimulation left cold.
Paperspeed 1 cm/sec. Time constant 10 sec.

Fig. 17

SUMMARY

In the review of literature we repeat some remarks about ageing in general followed by a survey of the embryology-anatomy of the inner ear. Presbyacusis is shortly dealt with, more detail is given with regard to vestibular function and its tests in children, adults, and old people. In this thesis we tried to gather some more objective data concerning vestibular function and age. Caloric nystagmus tests were administered to 250 healthy test subjects ranging in age from 10 tot 90 years. The nystagmus parameter used (maximum speed of the slow phase) revealed an increased responsitivity with age up to 40, followed by a decline. Age increments in nystagmus were more pronounced for warm stimuli than for cold. A possible explanation of the observed age effects is based on habituation, vascular influences, and vestibular nerve degeneration. A study of the variations concerning the main parameters which characterize the damped sinusoidal movement of the cupula-endolymphe system is presented. The torsion swing is described as well as the conditions of examination. Amongst the quantitative elements are distinguished the nystagmic frequency, the nystagmic amplitude, the speed of the slow phase and the quick phase of the nystagmus, as well as the nystagmic threshold. 395 people between 2 and 90 years of age were examined on a torsion swing, taking the nystagmus frequency as parameter. This showed variations depending on age-increase in responsitivity up to 60, followed after that age by a decrease. The next parameter was the amplitude, examined in another group of 77 subjects between 1 and 80 years of age. Here again we see variations in the size of the amplitude depending on age, mostly the reverse of the frequency, but very clearly marked, especially in the two extreme age-groups, so that the amplitude seems the best parameter when looking for age-differences in nystagmograms.
Testing another group of 113 test-subjects between 2 and 91 years old, the speed of the slow phase was followed, and an age-dependency was found when the results in the different age-groups were compared. The best vestibular reaction appeared in the young groups with a decline thereafter. More or less the same results were found after testing a different group of 72 subjects between 2 and 80 years, and following the speed of the quick phase in the different age-groups we can say that the quick phase is the parameter least affected by age-changes.
The last study concerned the nystagmic threshold for the semicircular canals. In a group of 122 subjects from 0—96 years we determined, on the torsion swing with increasing angular stimulation, the latency of the nystagmus. This value was found to be highest for people in their 80's, lowest in young children. These values decreased in people over 90, which would be in correspondence with the outcome of other investigators.

Die doel van hierdie proefskrif is om objektiewe gegewens met betrekking tot die verband tussen vestibulêre funksie en ouderdom te versamel. Die embriologie en anatomie van die binne-oor word beskryf met behulp van gegewens uit die literatuur, as ook presbiakusis.

Sowel die funksie as die toetse, bij kinders, volwassenes en bejaardes van die vestibulêre apparaat word bespreek.

Kaloriese toetse is afgeneem by 250 proefpersone tussen die ouderdomme van 10 en 90 jaar. Met die maksimum snelheid van die langsame fase as parameter, is tot en met die ouderdom van 40 jaar 'n duidelike toename in reaksies gevind. Na hierdie ouderdom is 'n afname daarin vasgestel. Hierdie aanvanklike toename gevolg deur afname van de kaloriese reaksie met toenemende ouderdom, was duideliker by die warm stimulasie as met koue prikkeling. As 'n moontlike verklaring van die met ouderdom saamhangende verskille word gewenning, vaatinvloede, of degenerasie van die vestibulêre senuwee aangegee.

'n Oorsig van die variasies van die belangrikste parameters wat tipies is vir die gedempte sinusoïde beweging van die kupula-endo-limfsisteem, wordt gegee. Die draaislinger word beskryf as ook die voorwaardes waaraan voldoen moet word om toetse met hierdie apparaat betroubaar te kan uitvoer.

Van de kwantitatiewe elemente word agtereenvolgens de frekwensie van die nistagmus, die amplitude, die snelheid van die langsame en snelle fases, as ook die drempelwaarde van die nistagmus beskou. Met die frekwensie van die nistagmus as parameter is 395 proefpersone tussen 2 en 90 jaar oud met die draaislinger getoets. Uit hierdie ondersoek blyk dat daar verskille is wat wel met die ouderdom saamhang: n.l. 'n toename van die reaksies tot aan die sestigste jaar, waarna 'n afname intree.

Die amplitude, as volgende parameter, is by 77 proefpersone, 1 tot 80 jaar oud, nagegaan. Ook hier is ouderdomsgebonde verskille opgemerk in die grootte van die nistagmus-amplitude, wat meestal die omgekeerde van die frekwensie was. Hierdie verskille was ooglopend, veral by die twee uiterste ouderdomsgroepe. Dit kom dus voor asof die amplitude die beste parameter is wanneer dit kom by die opsporing van leeftydsgebonde verskille in die nistagmogram.

By 113 proefpersone, 2 tot 91 jaar oud, is die snelheid van die langsame fase nagegaan. Ook hier is by die vergelyking van die resultate in die verskeie ouderdomsgroepe bevind dat daar 'n leeftijdsafhanklikheid bestaan. Dit toon aan dat die beste vestibulêre reaksies by jong mense verkry is en dat met toename in ouderdom daar 'n afname in die reaksies was.

Min of meer dieselfde bevindinge is verkry by 'n groep van 72 proefpersone, 2 tot 80 jaar oud; by hulle is die snelheid van die snelle fase nagegaan in die verskillende ouderdomme. In vergelyking met die ander parameters kom dit voor asof die snelle fase die minste leeftydsafhanklikheid vertoon.

Na 'n beskouing oor die drempelwaarde van die nistagmus vir die halfmaankanale, is 112 proefpersone, 0 tot 96 jaar oud, op die draaislinger aan 'n toenemende hoeksnelheid onderwerp, met bepaling van die latente periode van die nistagmus. Die waarde was die hoogste bij die persone van 80 jaar en ouer, die laagste by die jong kinders. Hierdie bepaalde waardes het weer kleiner geword by persone oor die ouderdom van 90 jaar. Hierdie resultate is in ooreenstemming met dié van ander ondersoekers.

SAMENVATTING

Het doel van dit proefschrift is objectieve gegevens te verzamelen betreffende het verband tussen vestibulaire functie en leeftijd. De embryologie-anatomie van het binnenoor wordt behandeld naar aanleiding van gegevens uit de literatuur, gevolgd door een beschouwing over presbyacusis. De functie — bij kinderen, volwassenen en oude mensen — van het vestibulaire apparaat met de bijbehorende onderzoekingen wordt besproken.

250 proefpersonen, variërend in leeftijd van 10-90 jaar werden calorisch onderzocht. Met de maximum snelheid van de langzame fase als parameter werd een duidelijke toeneming in reactie gevonden tot het veertigste jaar; na die leeftijd stelden wij afneming vast. Deze aanvankelijke toeneming en daarna weer afneming van de calorische prikkelbaarheid met het ouder worden was sterker uitgesproken bij de warme prikkeling dan bij de koude. Als waarschijnlijke verklaring van de waargenomen verschillen naar gelang van de leeftijd worden habituatie, vasculaire invloeden en degeneratie van de nervus vestibularis aangegeven.

Een overzicht wordt gegeven van de variaties in de voornaamste parameters welke de gedempte sinusoïdale beweging van het cupula-endolymphe systeem kenmerken. De torsieschommel wordt beschreven en de voorwaarden waaraan deze moet voldoen, teneinde het onderzoek met dit apparaat op verantwoorde wijze te kunnen uitvoeren.

Van de quantitatieve elementen worden achtereenvolgens de frequentie, de amplitudo, de snelheid van langzame en snelle fase en de drempelwaarde van de nystagmus nauwkeurig bekeken.

395 proefpersonen in de leeftijd van 2 tot 90 jaar werden op de torsieschommel onderzocht met de frequentie van de nystagmus als parameter. Uit dit onderzoek bleek dat er variaties zijn die met de leeftijd samenhangen: een toeneming van de reacties tot 60 jaar, en daarna weer een afneming.

Als tweede parameter werd de amplitudo gebruikt bij 77 proefpersonen tussen 1 en 80 jaar. Ook hier werden aan de leeftijd gebonden variaties opgemerkt in de grootte van de amplitudo van de nystagmus, welke meestal het omgekeerde was van de frequentie. Deze variaties waren duidelijk uitgesproken, vooral in de uiterste twee leeftijdsgroepen, zodat het lijkt of de amplitudo de beste parameter is wanneer het

er om gaat leeftijd-gebonden verschillen in de nystagmogrammen aan te duiden.

Bij 113 proefpersonen tussen 2 en 91 jaar werd de snelheid van de langzame fase nagegaan. Ook hier werd bij het vergelijken gevonden dat de resultaten afhangen van de leeftijd. Het bleek dat de beste vestibulaire reacties gemeten werden bij jonge mensen en dat met het ouder worden de reacties afnamen. Min of meer dezelfde resultaten werden gevonden bij 72 proefpersonen tussen 2 en 80 jaar. Bij hen werd de snelheid van de snelle fase nagegaan bij verschillende leeftijden. De snelle fase blijkt het minst afhankelijk te zijn van de leeftijd in vergelijking met de overige parameters.

Na een beschouwing over de drempelwaarde van de nystagmus voor de halfcirkelvormige kanalen, werd de latentietijd van de nystagmus bepaald. Hiertoe werden 122 proefpersonen tussen 0 en 96 jaar op de torsieschommel met toenemende hoeksnelheid onderzocht. De latentietijd bleek het hoogst te zijn bij personen ouder dan 80 jaar, het laagst bij jonge kinderen. De gemeten waarden werden weer kleiner bij mensen boven de 90 jaar, hetgeen zou overeenstemmen met de uitkomsten van andere onderzoekers.

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STELLINGEN

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Amsterdam, 5 oktober 1972

I

De fysieke en psychische gewaarwordingen, die bejaarden ondergaan bij het zingen in een koor, zijn te vergelijken met de sensaties van een persoon, die trimt.

II

Een nauwere band tussen militair-geneeskundige diensten en medische faculteiten schept de mogelijkheid tot het doen van wetenschappelijk onderzoek op een terrein, dat medisch moeilijk toegankelijk is. Daarnaast kunnen beide groepen winst boeken door vermindering van eenzijdigheid.

III

Een stapedectomie voor vliegend personeel dient te worden afgeraden.

IV

In research-instituten van universiteiten en hogescholen moeten de werktijden worden aangepast aan de experimenten en niet omgekeerd.

V

Ter verlichting van de administratieve en organisatorische taken van hoogleraren en lektoren is het belangrijk, dat hun afdelingen over een instituutsbeheerder beschikken.

VI

Er dient te worden voorkomen, dat onder druk van de publieke opinie op korte termijn op verschillende plaatsen in Nederland met coronairvaatchirurgie wordt begonnen zonder dat door een betrouwbare "pilot study" de resultaten eerder zijn geëvalueerd.

VII

Het is dringend gewenst van een gevaarlijke kruising een z.g. "block-crossing" te maken, waardoor na het oprijden, stilstand op zo'n kruising strafbaar moet worden gesteld.

VIII

In geval van de noodzaak tot postoperatieve beademing verdient het gebruik van de zgn. volume-limited machine de voorkeur boven de zgn. pressure-limited machine.

IX

Patienten met een mammacarcinoom groter dan 3 cm en palpabele okselklieren dienen behandeld te worden op die wijze welke de geringste morbiditeit geeft.