The human vestibulo-ocular reflex

effects of adaptation

Proefschrift

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aan mijn ouders en Anna

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ACKNOWLEDGMENTS

PREFACE

During my initial training as an ENT-surgeon at the University
Hospital Dijkzigt, Rotterdam, I examined many patients complaining of
various types of dizziness. It was usual to carry out a series of
clinical tests, selected according to the case history of the patient,
but they did not always lead to a clear diagnosis. Even when there
was a diagnosis, the pathogenesis and its relation to the physiology
of the vestibular system were seldom known. Furthermore, it appeared
to be difficult to differentiate between peripheral and central vesti-
bular disorders, a distinction which is of great importance for the
treatment.

A great deal of the knowledge about the functioning of the peri-
pheral vestibular system is drawn from the results of animal experiments
performed during the last few decades. In order to gain more insight
into the normal functioning of the human semicircular canals I decided
to investigate the vestibulo-ocular responses to various types of
angular acceleration in healthy subjects. The facilities required for
this investigation, a rotation room with a hydrostatic bearing and
sophisticated computer analysis programs, were already available at
Erasmus University. I had a longstanding interest in physics and
mathematics, both of which are essential for this type of research.
The ENT-department at Dijkzigt provided an atmosphere conducive to
investigation and experimentation, while my colleagues contributed
advice and encouragement. With these facilities I attempted to add
to the growing body of knowledge about the human vestibulo-ocular
reflex system.

GENERAL INTRODUCTION

The first understanding of the physiology of the semicircular canals of the vestibular organ dates from the late 19th century *(Henn and Young,* 1975). *Mach, Breuer* and *Crum Brown* all suggested that angular acceleration forms the specific stimulus for this organ. Due to inertia, the relative direction of flow of the fluid in the canals is opposite to that of the angular acceleration of the head. The sensory hair cells of the ampulla are deformed by the flow of endolymph and the stimulus input is transferred to the central nervous system. Postacceleratory reactions could not be explained by means of the Mach-Breuer-Crum Brown theory.

In the 1930's, *Steinhausen* (1933) demonstrated that the cupula was a jelly mass capping the crista of the ampulla, mechanically forming a single unit with the sensory cells and acting like a swing-door with its own elasticity. He also formulated the second order model for the displacement of the cupula, which functions like a highly damped pendulum.

The labyrinthine tone, first suggested by *Ewald,* was further elucidated by the discovery of resting discharges by means of single-fibre recordings *(Löwenstein and Sand,* 1940). The two-way response of the cristae could now be understood.

In the study of human vestibular function both sensation and the vestibulo-ocular reflex (VOR) are usually investigated. The VOR operates in a short reflex arc *(Gacek,* 1980); its three nerve cells lie in Scarpa's ganglion, the vestibular nuclei and the extra-ocular motor nuclei. The pathways of this reflex have been known for many years and the reflex has been used by vestibular physiologists as a qualitative and quantitative measure of vestibular function.
Van Egmond, Groen and Jongkees (1948) experimentally determined the time constants of the human VOR-system, using the second order model. Since the value of the long time constant T_1 of the VOR-system was found to be different from that of the vestibular sensation, an adaptation mechanism was proposed by *Groen* (1960). Its transfer function was derived by *Young and Oman* (1969) and *Malcolm and Melvill Jones* (1970).

Attenuation of the VOR-response has frequently been observed in experiments. This attenuation can be ascribed to fatigue, habituation and adaptation, but a clear distinction has often not been made between these words. This has led to confusion.

The VOR-system is a modifiable system which adjusts to a variety of situations and stimuli. Although the system can accommodate in either direction, due to the nature of the experiments used to investigate specific responses, the accommodation which is usually observed gives rise to attenuation of the response.

Fatigue can be described as a temporary state of exhaustion. Brief intervals of rest are usually sufficient for the subject to recover from fatigue and for the attenuation of response to disappear. Lack of alertness as a cause of attenuation of response also falls within this category. Conversely, the VOR-response can be augmented by increasing

alertness through mental exertion or the administration of appropriate drugs.

The reduction in response due to repeated stimulation is called habituation or long-term adaptation. There is not a simple decrease in the response: instead the original response becomes more and more inhibited as the opposing reaction becomes more fully developed. A central process probably accounts for this active modification. The phenomenon of pattern-building, as described by *Groen* (1960), is a form of habituation. Other forms of habituation are seen in the fact that the VOR can be modified by changes in the input from both the visual system *(Collewijn*, 1979) and the proprioceptive system.

Adaptation, by which is meant short-term adaptation, is a special type of decline in response, situated within the reflex arc. It occurs during a prolonged stimulus and its location is probably more peripheral, although central processes also have their influence on the adaptation mechanism.

The definitions of the above three terms were drawn, in part, from *Collins* (1974) and are those used in this thesis.
Finally it should be mentioned that the VOR-system has close connections with the reticular formation, the myelum, the cerebellum and the cerebrum, all of which influence each other in reciprocal ways.

This thesis systematically investigates the influence of adaptation on the human VOR-response. Various types of angular acceleration around the vertical axis are used to determine the time constants of the VOR-system. Care is taken as far as possible to avoid fatigue, habituation and the effects due to the order in which the experiments were done. Since each chapter was written as a paper dealing with a specific subject, the accompanying description of the problems under investigation and the references are contained within the chapters.
In section I impulsive stimuli are used.
The intra-subject variance and the inter-subject variance are investigated in chapter I. In chapters II and III the influence of the adaptation mechanism on the long time constant of the VOR is determined theoretically and experimentally.
In section II sinusoidal stimulation is used.
The theoretical and experimental frequency response of the VOR is described in chapters IV and V, and the effect of adaptation is determined at low frequencies.
In section III constant angular acceleration is used as a stimulus. In chapter VI the theoretical response is calculated, while in chapter VII the results are given for a small group of subjects. These are not yet fully understood.
The descriptions of the experiments are followed by a general discussion concerning the type of stimulus which appears to be the most suitable for the investigation of adaptation, and the extent to which the second order model with adaptation can account for the results obtained with the various stimuli.
The appendix contains a comprehensive description of the deriva-

tion of the equations used.

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SECTION I: IMPULSIVE STIMULATION OF THE HUMAN VOR-SYSTEM

CHAPTER I: STATISTICAL EVALUATION OF NYSTAGMUS IN CUPULOMETRY

ABSTRACT. The literature on cupulometry shows inconsistent data as to (1) the magnitude of the time constant T_1; (2)the inter-subject variance; (3)the difference in T_1 between clockwise and counter-clockwise rotation, and (4)the linearity of the system. In our investigations, the nystagmus was measured after a step in angular velocity. All tests were carried out six times for 5 subjects. The time constant T_1 was calculated from the slope of the decay of the slow phase eye velocity. Statistical evaluation of the results showed: an intra-subject variance which is greater than the inter-subject variance; significant differences between subjects; mean values of T_1 for clockwise and counter-clockwise rotation of 13.2 s (SD=1.4 s) and 12.8 s (SD=1.7 s) respectivily; a significant difference of T_1 between clockwise and counter-clockwise rotations for individual subjects at the 95% confidence interval level; no relation between T_1 and the amplitude of the step in angular velocity, and a linear increase of the maximum slow phase eye velocity with the amplitude for velocities below 100 $^\circ$/s, whereas at higher velocities saturation occurs.

INTRODUCTION

The forces generated within the semicircular canals by rotational stimuli can be calculated precisely. As a consequence, our knowledge of the physical characteristics of the canal mechanism in normal human beings has made great advances.

In cupulometry - an experimental technique introduced by *van Egmond et al.*(1948) - the reactions of the vestibular system are observed after a sudden start or stop (a step in angular velocity). Analysis of the vestibular reaction can lead to statements about the linearity of the system, differences between clockwise (CW) and counter-clockwise (CCW) rotation and both the intra-subject variance and the inter-subject variance. The literature on cupulometry shows many inconsistencies in the measured values of the vestibular reactions.

Van Egmond et al.(1948, 1949) determined the time constant T_1 from the duration of nystagmus, after a step in angular velocity. From these studies T_1 was found to be 16 s *(Groen,* 1956). *Keser* (1950) found no increase in the maximum slow phase eye velocity (MSPV) above 120 $^\circ$/s. There was no difference of T_1 between CW and CCW stimulation, although in general a second trial showed less nystagmus than a first. He found large inter- and intra-individual differences.

Melvill Jones et al.(1964) determined T_1 from stimuli in the yaw, pitch and roll planes of the head. For yaw they found T_1=15.6 s (SD=0.6 s). The very small standard deviation is remarkable (N=8). *Brown and Crampton* (1964) used a constant acceleration as a stimulus as did many others. After the termination of this acceleration (duration 9 s), they observed an exponential decay of slow phase eye velocity (SPV). The time constant of this decay was 15.5 s as pointed out by *Guedry* (1974). They did not find T_1 to vary with the stimulus amplitude. *Stark* (1964) determined T_1 from the decay of nystagmus after a sudden stop. She found a mean value of 14.8 s, with a range from 9.2 s to 24.0 s. There were significant differences between subjects; for a given sub-

ject, T_1 was found to be independent of the amplitude of the impulse. The MSPV increased linearly with the amplitude of the velocity step, with a gain of 0.8.

Benson (1970) used a 60 °/s step in velocity as stimulus. He found T_1 to be 17.8 s. *Simon et al.* (1975) studied the quick phase of the post-rotatory nystagmus in 35 healthy subjects. The mean values of various parameters were determined but great variation in the responses was found. These authors also found great differences of T_1 between CW and CCW rotation. *McClure et al.* (1976) found a variation of the time constant T_1 from 7 s to 35 s for healthy subjects, and also that vestibular asymmetry was not uncommon. *Konrad et al.* (1976) and *Sills and Honrubia* (1978) found that the MSPV is the best indicator of the variables examined. Their figures show a linear increase in MSPV with impulse amplitudes up to 128 °/s. The time constant determined from the decay of nystagmus generated by a step in angular velocity was found to be 16.6 s (SD= 5.5 s) for a stimulus of 256 °/s, and 18.2 s (SD=6.6 s) for a stimulus of 128 °/s. These two values do not differ significantly.

The results cited above are summarized in table I. This table shows a great range of the time constant T_1. All investigators, except *Melvill Jones et al.* (1964), found a large standard deviation. The results of the difference in T_1 between CW and CCW rotation and of the linearity of the system are inconsistent. All this compelled us to raise the following questions:

    (a) Is the fact that some investigators have found inter-indivi-
        dual variation in T_1 and others have not, due to inaccuracy
        of the measurements or is this variation a reflection of real
        differences between subjects?
    (b) Are the differences of T_1 between CW and CCW stimulation real?
    (c) Is the system linear?(In which case the time constant T_1
        is independent of the stimulus.) And if so, does the MSPV
        increase linearly with the amplitude of the stimulus?

In an effort to answer these questions, we examined the following parameters of nystagmus after a step in angular velocity: the time constant T_1 of the decay in SPV, and MSPV. The duration of the nystagmus and the possible presence of after-nystagmus are not dealt with in this chapter (see chapter II and III).

METHOD

The stimulus
The stimulus was an angular acceleration pulse (step in angular velocity) administered by a rotation room *(Rodenburg and Teerhuis,* 1975; *Teerhuis et al.,* 1979). Thanks to the elimination of coulomb friction by use of a hydrostatic bearing, the room will follow the drive pattern smoothly, even at very low velocities and zero crossings. An electro-hydraulic servomotor drives the room via a belt. This motor is control-led by a small electrical signal from a function generator, permitting the realization of a great variety of stimuli. The room can be stopped or started in about two seconds (see fig. 1). Maximum acceleration is 120 °/s².

Table I. Cupulometry results taken from literature

Authors	Time constant T_1 in seconds	CW/CCW rotation	MSPV linearity	T_1 independent of amplitude	Variability of T_1
van Egmond et al.(1948, 1949) Groen (1956)	16				
Keser (1950)		no difference	no, saturation 120 o/s		large
Melvill Jones et al.(1964)	15.6 SD=0.6				small
Brown and Crampton (1964)	15.5			yes	
Stark (1964)	9.2-24.0		yes	yes	large
Benson (1970)	17.8				
Simon et al. (1975)		great difference			large
McClure et al. (1976)	7-35	difference			large
Konrad et al. (1976)	16.6 SD=5.5				
Sills and Honrubia (1978)	18.2 SD=6.6		yes	yes	large

Recording

The live electrodes were taped near the outer canthi of the eyes, and the ground electrode to the middle of the forehead. The electro-oculographic signals were amplified by a Tektronix TM 502 amplifier with

the following characteristics: common mode rejection, 100 dB; input impedance, 100 MΩ; gain $5x10^3$; frequency response, DC–100 Hz. The amplified signals were recorded on magnetic tape by a Bell & Howell 4010 recorder with AD 8 PCM system (4 channels; frequency response, DC–70Hz). The signals were also recorded on paper by a Siemens Oscillomink-L recorder; frequency response, DC–1.250 Hz.
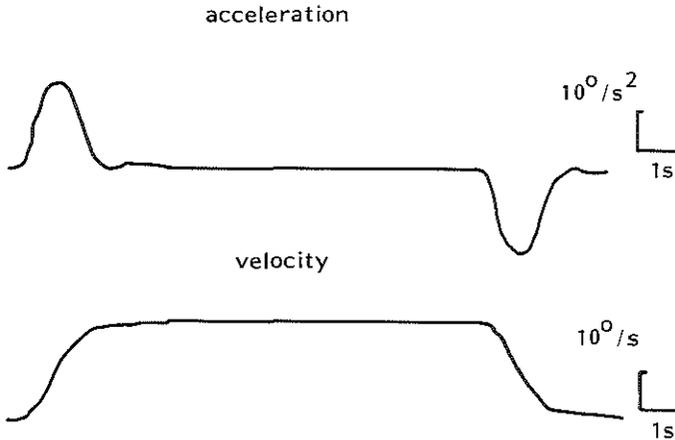
Fig. 1. Recording of the stimulus.
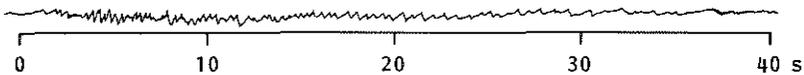
Fig. 2. Recording of the nystagmus after a 142 °/s step in angular velocity.

Subjects and procedure

All tests were carried out on 5 young and healthy subjects without oto-neurological history or vestibular experience.

The subject sat in a chair with his vertex at the centre of rotation and his head fixed upright in a holder. The movement of the head was measured by using a coil in a magnetic field (according to *Robinson*, 1963). The coil was fixed to a bite-board while the head of the subject was fixed in the usual way. The measurements showed that the position of the head changed slowly. This variation was maximal 25 minutes of arc. During the greatest amplitude (142 °/s) a movement of the head was measured of only 25 '/s. From this measurement it was concluded that

the fixation of the head was adequate.

The experiments were performed with the subjects' eyes open in the dark. Subjects were kept alert by giving them mental arithmetic. Each subject was tested in six sessions. The subjects' direction of rotation was alternated from one test to the next. Within each test a start was always followed by a stop. After such an acceleration pulse, a rest period of at least 3 min was given. Always starting with the lowest, three amplitudes of velocity steps were used: 50, 100 and 142 °/s. Although 60 °/s is advised as maximal stimulus in clinical cupulometry, we also used much greater amplitudes to examine whether the T_1 is smaller for these higher amplitudes.

Since the experimental conditions for a start were exactly the reverse of those for a stop, we could distinguish between CW and CCW stimulation without making any further corrections.

Data Processing

The slow phase velocity was determined by hand from the paper recordings. An example of a recording is given in fig. 2. The SPV was plotted on a logarithmic scale. The decay of SPV is linear on this scale, and a straight line through the experimental points was drawn by eye. The time constant T_1 was determined from the slope of this line. This method gave practically the same results as curve fitting with the aid of a small table computer.

RESULTS

Fig. 2 shows an example of a nystagmus found after a sudden stop. The SPV is maximum after about 6 s, and then increases to zero in about 40 s. As mentioned above, after-nystagmus will not be considered here. The SPV is plotted on a linear scale in fig. 3 and on a logarithmic scale in fig. 4.

Subject AS
date 6-1-78
stimulus: start + 142 °/s
T_1 = 10.4 s
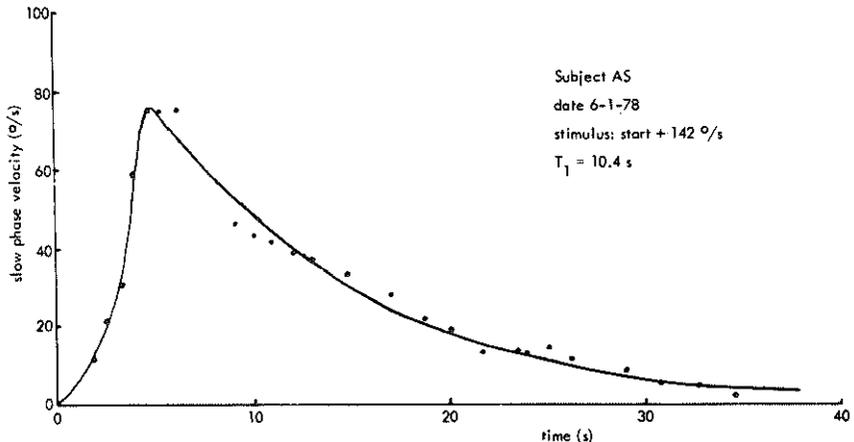
Fig. 3. Slow phase eye velocity (SPV) after a 142 °/s step in angular velocity. The ordinate is linear.   Exponential curve with a time constant of 10.4 s.

Subject AS
date 6-1-78
stimulus: start + 142 °/s
a = 126
b = -0.96
T_1 = 10.4 s
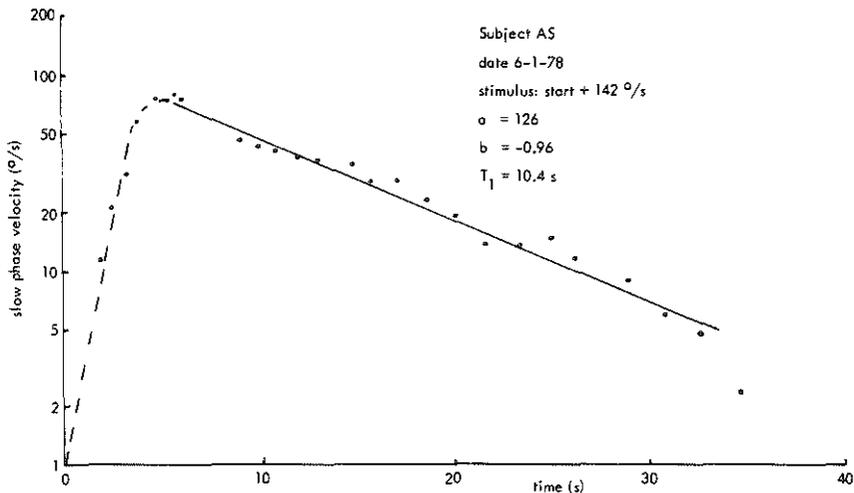
Fig. 4. Slow phase eye velocity (SPV) after a 142 °/s step in angular velocity. The ordinate is logarithmic. Solid line: straight line with a time constant of 10.4 s. Fig. 3 and fig. 4 represent the same test.

The decay is found to have a time constant T_1 of 10.4 s in this example.

The time constant T_1 was determined for angular velocity steps of 50, 100 and 142 °/s. The results are presented in fig. 5 for both CW and CCW rotation. The mean values of T_1 lie between 10 s and 18 s.

The maximum amplitude of SPV as a function of the amplitude of the step in velocity is presented in fig. 6. This figure shows a linear relation for amplitudes below 100 °/s.

DISCUSSION

After a step in angular velocity, the SPV of the nystagmus is maximum at about 6 s and then decreases exponentially. *Stark* (1964) found that the decay is more than exponential after 27 s. We also found this in some cases, but very often the decay remained exponential until 40 s after the stop or start, when the SPV is so small (4-5 °/s) that it is impossible to determine the decay with any degree of accuracy. The mean values of T_1 for individual subjects lie between 10 s and 18 s for all experimental conditions used here. The mean value of T_1 for all subjects for CW rotation is T_1=13.2 s (SD=1.4 s) and for CCW rotation is T_1=12.8 s (SD=1.7 s).

If several subjects are tested once each, as is usually done, the difference of their responses is interpreted as a variation between subjects. However, this could be incorrect. The observed variation could arise from two sources:

20
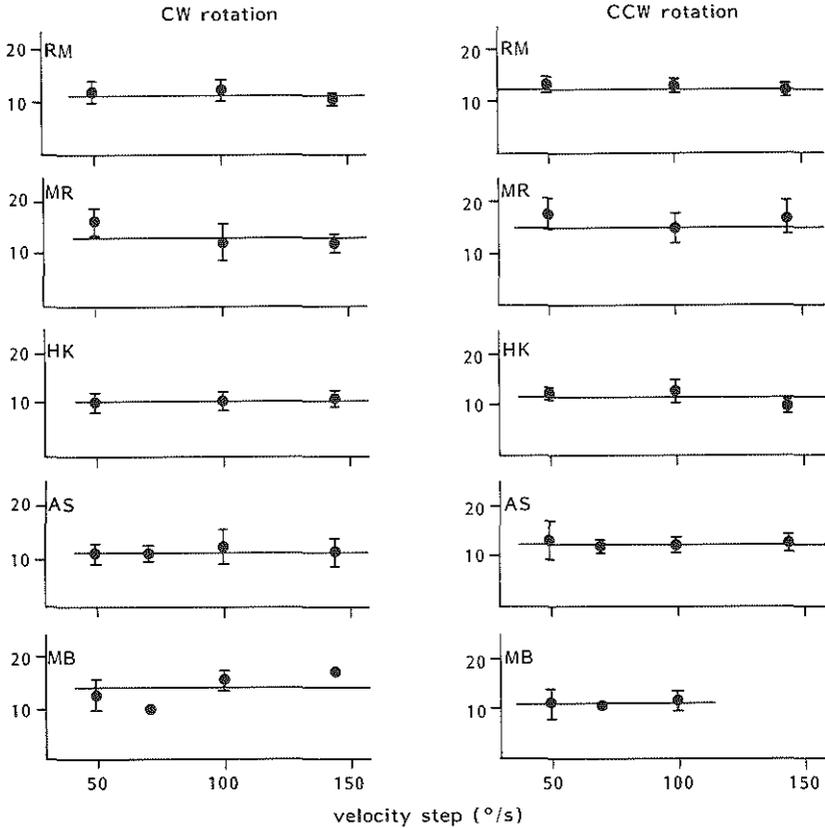
*Fig. 5. The time constant T₁ for the 5 test subjects, with steps
in angular velocity of 50, 100 and 142 °/s and both CW and CCW rotation.
The bar shown round each experimental point has a width equal to twice
the standard deviation.*

The first might reflect a real difference between subjects. This varia-
tion is called the inter-subject variance.

Secondly, if each subject is tested only once, the response recor-
ded may be unique and not reflect the more usual responses of that
subject. If one subject is tested repeatedly with the same test any
difference in the responses can be called the intra-subject variance.
Responses can also vary if the test utilized is unreliable or if the
subject is inconsistent in his responses for reasons other than those
being tested.

The fundamental theorem of the analysis of variance says that
the total sum of squares, that measures the variations of each subject's
responses to each test, can be devided into a component sum of squares

that measures the variation in responses due to subjects being different
from each other (inter-subject variance) and one due to a subject beha-
ving differently from test to test (intra-subject variance). The relative
magnitude of the inter-subject and the intra-subject variance can be
estimated by testing a number of subjects several times each.
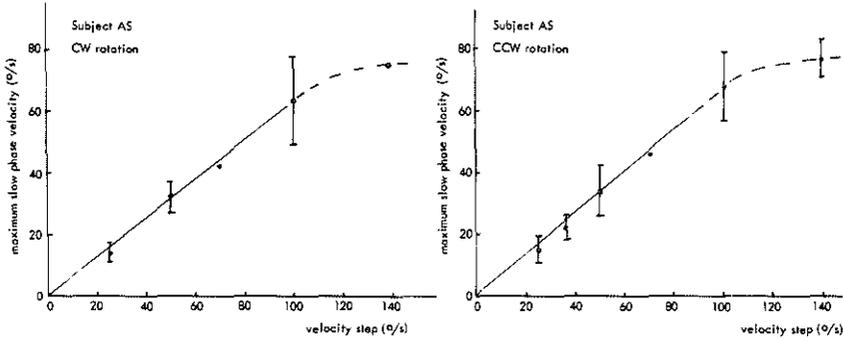
Fig. 6. Maximum slow phase eye velocity (MSPV) as a function of
stimulus amplitude for CW and CCW rotation. Bar is 2xSD.

The results of this analysis are given in table II, where it is
shown that the intra-subject variance is greater than the inter-subject
variance.

The range for the value of the time constant T_1 is relatively
wide (7 s-25 s), but comparable with what was found by *Stark* (9.2 s-
24.0 s) and *McClure et al.* (7 s-35 s). However, they did not distinguish
intra-subject variance and inter-subject variance. Our analysis shows
that the inter-subject variance is smaller than the variance, they ob-
served.

Table II. The mean value of T_1, the intra-subject variance (σ_f),
the inter-subject variance σ_d and 95% confidence interval for σ_d.

Rotation	T_1	σ_f	σ_d	95% confidence interval for σ_d
CW	13.2	2.0	1.4	$0.5 < \sigma_d < 4.4$
CCW	12.8	2.2	1.7	$0.7 < \sigma_d < 5.2$

The mean values of T_1 for all subjects do not differ for CW and
CCW rotation. If their values are compared for individual subjects,
differences are found. The 95% confidence interval for the diffenrence
in T_1 between CW and CCW rotation ($\mu_1 - \mu_2$) are shown in table III.
When the upper limit of the confidence interval was positive
and the lower negative, so that the confidence interval contained

zero, we assumed that the difference was not significant. In all other cases, we took the difference in T_1 to be significant.

Table III. 95% confidence interval for the difference in T_1 between CW and CCW rotation

Subject	95% confidence interval for $\mu_1-\mu_2$	Significant difference
RM	$-1.9<\mu_1-\mu_2<0.9$	no
MR	$-4\ \ <\mu_1-\mu_2<-\ 2$	yes
HK	$-3.7<\mu_1-\mu_2<-0.3$	yes
AS	$-3.6<\mu_1-\mu_2<+3.2$	no
MB	$+2.7<\mu_1-\mu_2<+5.3$	yes

When the difference $\mu_1-\mu_2$ is significant, it can be either possitive or negative. Part of the disagreement whether there are differences in T_1 between CW and CCW rotation can be explained by the fact that some investigators compared individual data and others the mean values for their subjects. Since the difference in T_1 between CW and CCW can be positive or negative, the difference between the mean values for a number of subjects will be much smaller.

Table IV. 95% confidence interval for B

Subject	Direction	95% confidence interval	The 95% confidence interval contains B=o
RM	CW	$-0.026<B<0.032$	yes
	CCW	$-0.029<B<0.006$	yes
MR	CW	$-0.079<B<-0.011$	no
	CCW	$-0.069<B<\ 0.024$	yes
HK	CW	$-0.030<B<0.013$	yes
	CCW	$-0.041<B<0.011$	yes
AS	CW	$-0.049<B<0.064$	yes
	CCW	$-0.056<B<0.039$	yes
MB	CW	$-0.012<B<0.079$	yes
	CCW	$-0.021<B<0.044$	yes

The question whether the time constant T_1 does vary within the amplitude range used was examined by applying linear regression analysis. If the coefficient B of the regression line is zero, T_1 is independent of the amplitude.

The 95% confidence intervals for B were determined. If this in-

terval contains B=o, the hypothesis B=o cannot be rejected. Table IV
shows the results of these calculations. In all but one case the hypo-
thesis B=o could not be rejected. So it may be concluded that the time
constant T_1 does not vary within the amplitude range investigated.
This is in agreement with the results of *Brown and Crampton* (1964) and
Sills and Honrubia (1978).

   The MSPV increases linearly with the amplitude up to 100 °/s.
For most of the subjects, saturation appears at higher amplitudes. The
mean gain (ratio of MSPV and step in angular velocity) for our 5 subjects
was 0.66 which is lower than the value of 0.8 found by *Stark* (1964).

   We have not distinguished between the time constant T_1 and the
time constant T_a due to adaptation. Adaptation will tend to lower the
calculated time constant; our values will thus be less than those ac-
cording to the pendulum model (see chapter II and III).
   In view of the great intra-subject variance, determination of T_1
does not seem suitable for distinguishing between normal and pathological
subjects. *Sills and Honrubia* (1978) found the same distribution for two
groups of patients, viz. one group with unilateral vestibular lesions
and one group with tumors of the cerebellopontine angle, as for normal
subjects. However, other parameters can be of diagnostic value. *Konrad
et al.*(1976) showed that differences between CW and CCW can define a
normal range and that patients with unilateral lesions are outside that
normal range. These authors also found increased responses in patients
with primary cerebellar disease. It may thus be possible to use cupulo-
metry to provide information about the location of lesions.

   CONCLUSIONS

   The decay of SPV after a step in angular velocity was found to
be exponential. The time constant, T_1, of this decay was found to be
13.2 s (SD=1.4 s) for CW and 12.8 s (SD=1.7 s) for CCW rotation. The
intra-subject variance is greater than the inter-subject variance. The
time constant T_1 for a given subject can be different for CW and CCW
rotation. This difference can be positive or negative. The system is
found to be linear up to a certain stimulus level: (a)T_1 does not
depend on the amplitude of the step in angular velocity; (b) the MSPV
increases linearly with the amplitude of the step in angular velocity
below 100 °/s, while above 100 °/s saturation occurs.

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CHAPTER II: INFLUENCE OF ADAPTATION UPON THE IMPULSIVE TIME CON-
STANT OF THE HUMAN VESTIBULO-OCULAR REFLEX (VOR) SYSTEM

I. THEORETICAL STUDY

ABSTRACT. From the impulse response of the human vestibulo-ocular
reflex system the value of the long time constant T_1 can be calculated
in two different ways: (a) by plotting the decay of the response on log-
linear graph paper, or (b) by plotting the duration of the response
against the logarithm of the impulse amplitude for various impulse
amplitudes, i.e. the cupulometric method. By means of mathematical mo-
dels, with and without adaptation, the effect of the two methods of
calculation on the value of the response T_1 was determined. The adap-
tation term was demonstrated to give a distinct reduction in the value
of the response T_1 compared with that of the cupular T_1, especially
when the cupulometric method (b) was used. The extent of this reduction
was calculated.

INTRODUCTION

In the investigation of the function of the horizontal semi-
circular canal, the interpretation of the experimental data is based
on two fundamental assumptions:
1.   the mechanics of the cupula-endolymph system can be regarded as
     a heavily damped torsion pendulum, and hence be described as a
     second order system. Its transfer function is determined by two
     time constants:
     - T_1, the long time constant of cupular restoration;
     - T_2, the short time constant, which is an indicator of the mode
       of reaction of the system to an impulsive stimulus;
2.a   vestibular sensation and angular velocity of the slow phase
      nystagmus are both proportional to cupular displacement, θ_c.
The long time constant T_1, calculated from cupulograms of vestibular
sensation, appears to differ considerably from that calculated for
nystagmus *(van Egmond et al.,* 1948). To explain this difference a
centrally located inhibitory mechanism was proposed by *Groen* (1960).
The introduction of this short term adaptation mechanism as it is called,
invalidates assumption (2.a) which must be replaced by:
2.b   the vestibular response (sensation and nystagmus) is proportional
      to the difference between cupular displacement θ_c and a constantly
      shifting zero-velocity reference level R *(Young and Oman,* 1969;
      Malcolm and Melvill Jones, 1970). The adaptation time constant Ta
      describes the rate of movement of this reference level. The value
      of T_a is different for sensation and nystagmus.
Adaptation tends to reduce the value of the long time constant T_1 cal-
culated from experimental data on the vestibular response (response
T_1) in comparison with the long time constant of cupular restoration
(cupular T_1).

The response T_1 of the VOR-system to an impulsive stimulation
can be calculated in two different ways:

(a) by plotting the velocity of the slow phase nystagmus on log-linear
     graph paper and determining the decay, or
(b) by plotting the duration of the post-rotatory nystagmus against
     the logarithm of the impulse amplitude for various impulse ampli-
     tudes, i.e. cupulometry *(van Egmond et al., 1948)*.
Young and Oman (1969) stated that after a short stimulation the slow
phase eye velocity curve decays with practically the same time constant
as the cupular deflection. In agreement with *Groen* (1960) we should
expect more pronounced evidence of the adaptation effect, but this has
not yet been demonstrated.

     The present study has been carried out to answer the following
questions:
(1) does adaptation have an effect on cupulometric data and the
     calculation of the response T_1, and if so: to what extent?
(2) does the value of the response T_1, obtained from calculations made
     by the cupulometric method (b), differ systematically from the
     value of the response T_1, obtained by the decay method (a)?

METHOD AND RESULTS

     We have therefore calculated the responses to impulsive stimulation
of the pure second order model and of the second order model with adap-
tation, in order to investigate the effects of adaptation and of the
two different methods of calculation on the value of the response T_1.
The reader is referred to the APPENDIX for a comprehensive description
of the equations used.

   a. Second order model
     In physical terms the movement of the cupula in the semicircular
canal system is governed by three properties:
     I=moment of inertia of the endolymph;
     B=damping torque, determined by the viscosity of the endolymph;
     K= elastic torque, determined by the stiffness of the cupula.
The relation between the applied angular head acceleration, $\ddot{\theta}_h$, and the
angular displacement of the cupula, θ_c, is given by the following second
order differential equation:

$$I\ \ddot{\theta}_h(t) = I\ \frac{d^2\theta_c}{dt^2} + B\ \frac{d\theta_c}{dt} + K\theta_c \tag{1}$$

In Laplace notation, the linear transfer function of this system is:

$$H(s) = \frac{\theta_c(s)}{\ddot{\theta}_h(s)} = \frac{I}{Is^2+Bs+K} = \frac{k}{(T_1s+1)(T_2s+1)} \tag{2}$$

where $k=I/K=T_1.T_2$; $T_1+T_2=B/K$; since the damping range is large, T_1 and
T_2 are approximately equal to $T_1=B/K$ and $T_2=I/B$. In the case of heavy
viscous damping and a stimulus amplitude of unity, the response of the
system to a step change in angular velocity (impulse) will be:

$$\theta_c(t) = o \qquad\qquad \text{for } t=<o$$

$$\theta_c(t) = \frac{T_1.T_2}{T_1-T_2}\ (e^{-t/T_1}-e^{-t/T_2}) \qquad \text{for } t > o \tag{3}$$

The response of this second order model, simulating the slow phase eye

velocity according to assumption (2.a), was computed in order to calculate the value of the response T_1. For this reason equation (3) has been programmed and multiplied by various stimulus amplitudes; the cupular time constant T_1 is chosen as 20 s and T_2 as 0.01 s. The responses are plotted in fig. 1. The maximum response value is reached at 0.07 s and the decay approaches the abscissa asymptotically.
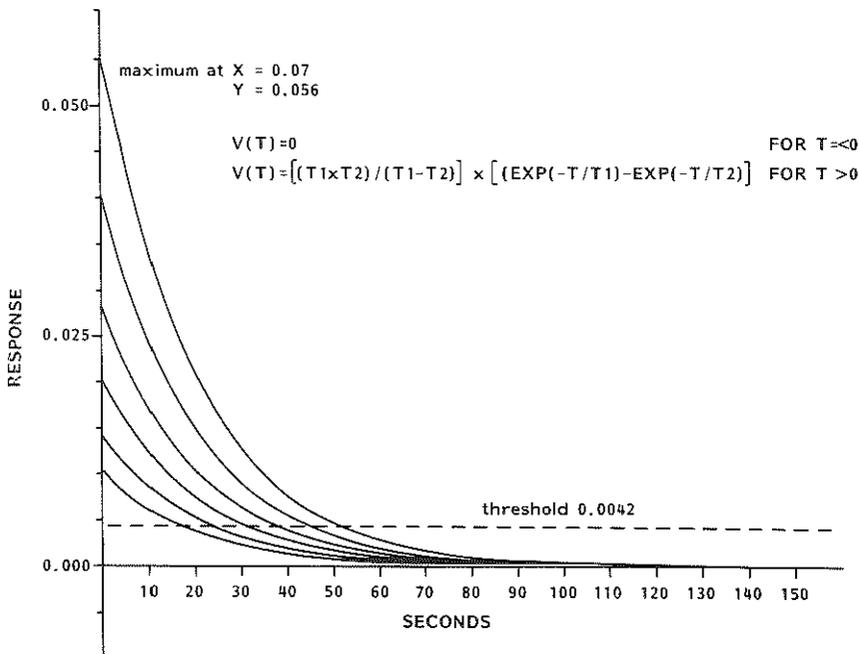
Fig. 1. Response of the second order model after an impulsive stimulation with amplitude factor 1, 1.4, 2, 2.8, 4 and 5.6. Threshold value is 7.5% of the maximum response. Cupular T_1=20 s, T_2=0.01 s.

In fig. 2 the responses are given on log-linear graph paper. The value of the response T_1 is calculated by the decay method (a), and is indeed equal to the inserted cupular T_1 (20 s).

For the application of the cupulometric method (b) it is necessary to assume a response threshold when determining the duration of response for various impulse amplitudes. Without a threshold all response durations are infinite. In fig. 1 the threshold is chosen as 7.5% (0.0042 units) of the maximum response (0.056 units). Plotting the duration of response until the threshold is reached (for 4 different thresholds) against the logarithm of impulse amplitude, results in parallel curves (fig 3). The calculation of the response T_1 yields again the value of 20 s for the cupular time constant T_1, for all thresholds.

Conclusion: The calculation of the response T_1 from the response of the second order model without adaptation gives the value of the inserted cupular T_1, regardless of the method of calculation. The value

chosen for the threshold in the cupulometric method has no effect on the result.
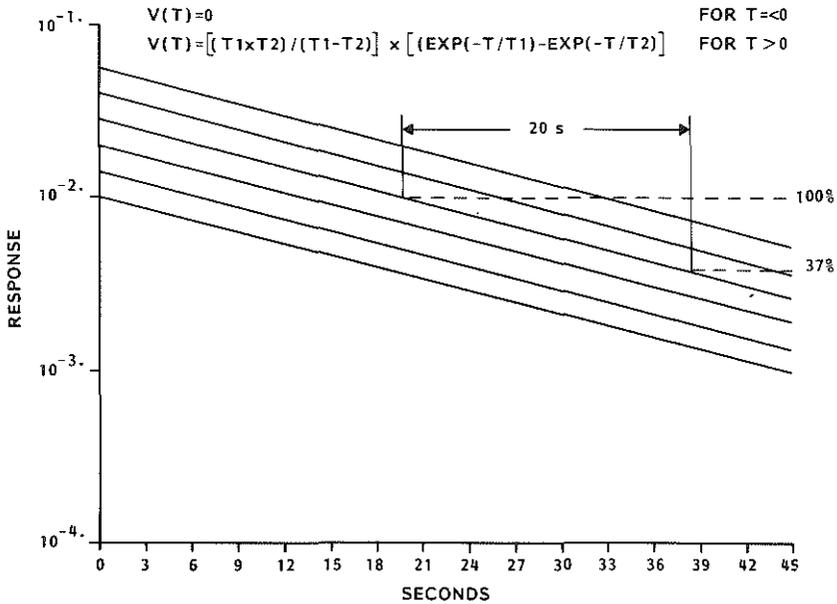
Fig. 2. Same as fig. 1, plotted on log-linear graph paper. The value of the response T_1, calculated by the decay method (a), is also 20 seconds.

$V(T)=0$ FOR $T \leq 0$

$V(T) = [(T1 \times T2)/(T1-T2)] \times [(EXP(-T/T1)-EXP(-T/T2)]$ FOR $T > 0$
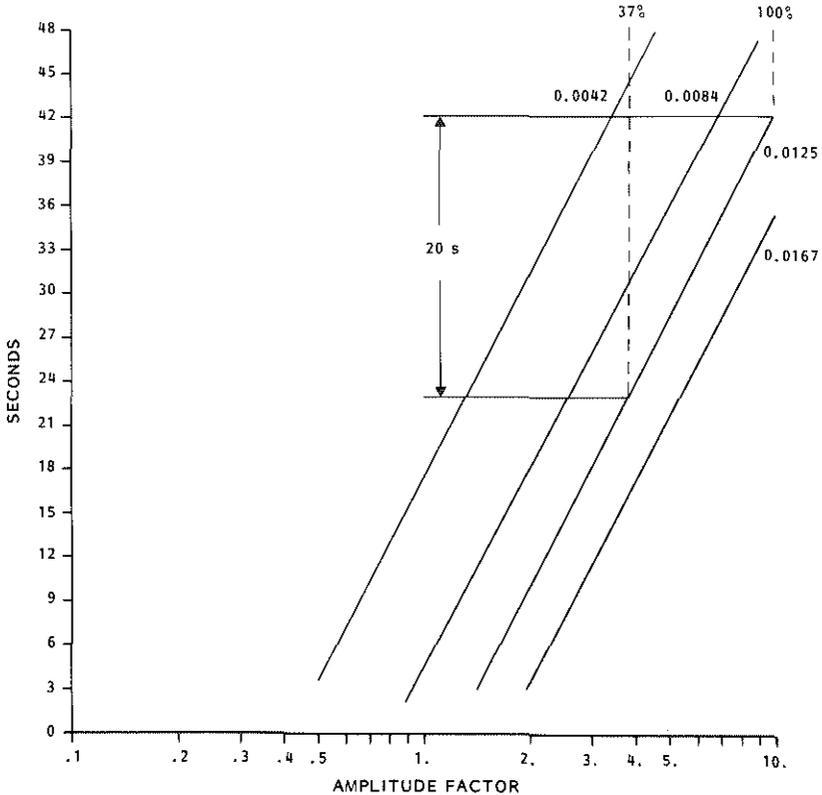
Fig. 3. Response duration until the threshold is reached, plotted against the logarithm of the impulse amplitude. Second order model, cupular $T_1=20$ s; $T_2=0.01$ s. Thresholds: $0.0042=7.5\%$; $0.0084=15\%$; $0.0125= 22.5\%$; $0.0167=30\%$ of the maximum response. The value of the response T_1, calculated by the cupulometric method (b), is also 20 seconds.

b. Second order model with adaptation

Although starting from different assumptions the resulting transfer function of the adaptation mechanism (H_a) is the same both for the model of *Young and Oman* (1969) and for that of *Malcolm and Melvill Jones* (1970):

$$H_a(s) = \frac{\dot{\theta}_e(s)}{\theta_c(s)} = \frac{T_as}{T_as+1} \tag{4}$$

where $\dot{\theta}_e$=angular eye velocity.

Combining the second order model and the adaptation model, the overall function is:

$$H(s) = \frac{\dot{\theta}_e(s)}{\theta_h(s)} = \frac{T_1 \cdot T_2 \cdot T_as}{(T_1s+1)(T_2s+1)(T_as+1)} \tag{5}$$

The response of this function to a step change in angular velocity (impulse) will be:

$$\dot{\theta}_e(t)=0 \qquad\qquad\qquad \text{for } t=<0$$

$$\dot{\theta}_e(t)= \frac{T_1 \cdot T_2 \cdot T_a}{T_1-T_2} \{ \frac{1}{T_a-T_1} \cdot e^{-t/T_1} - \frac{1}{T_a-T_2} \cdot e^{-t/T_2}$$

$$+ (\frac{1}{T_a-T_2} - \frac{1}{T_a-T_1}) \cdot e^{-t/T_a} \} \qquad \text{for } t > 0 \tag{6}$$

This equation (6) has also been programmed and multiplied by various impulse amplitudes. The values of cupular T_1, of T_2 and of T_a are chosen as 20, 0.01 and 100 s respectively, which are close to the values found in the literature (see discussion). The response curves, simulating the slow phase eye velocity according to assumption (2.b), are shown in fig.4.

A comparison of fig. 4 with fig. 1 shows three pronounced differences:
(1)   the slope of the decay has become steeper;
(2)   the curves pass through the zero-response level and reveal a prolonged phase of reversed response;
(3)   all curves cross the zero-level at the same moment, t_o, for a given set of time constant values.
The maximum response amplitudes in fig. 1 and fig. 4 are equal.

In fig. 5 the responses are plotted on log-linear graph paper, using method (a). The curves are not straight and the decay is faster than exponential. The value of the response T_1 can only be estimated from such a plot. This has been done by drawing a tangent to the upper curve in the time range where the slow phase eye velocity after an impulsive stimulation is measured: from about 6 to 26 seconds (*Boumans et al.*, 1980, chapter I). In fig. 5 the estimated value of the response T_1 is found to be 13.8 s.

We have also studied the effect of varying the values of the cupular T_1 and of the adaptation time constant T_a on the calculation of the long time constant of the response (table I). The estimated value of the response T_1 is always lower than the value of the cupular T_1 inserted in equation (6). The reduction in the response T_1 appears to be less where the value of the cupular T_1 is low and where the adaptation time constant is large.

The value of the response T_1 can also be estimated by the cupulo-metric method (b). The duration of the response until it reaches the threshold is plotted (for 4 threshold values) against the logarithm of the impulse amplitude (fig. 6). Response T_1 is estimated by drawing the best fitting line through the points corresponding to stimulus

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$$V(T)=0 \qquad \text{FOR } T =< 0$$
$$V(T)=T1 \times T2 \times \left[(TA/(T1-T2))\right] \times \big[\{1/(TA-T1)\} \quad \times \text{EXP}(-T/T1)- $$
$$\{1/(TA-T2)\} \quad \times \text{EXP}(-T/T2)+$$
$$\{1/(TA-T2)-1/(TA-T1)\} \times \text{EXP}(-T/TA)\big] \quad \text{FOR } T > 0$$

maximum at X = 0.07
Y = 0.056

0.050

0.025

RESPONSE

Y=0 X=40.50

0.000

10 20 30 40 50 60 70 80 90 100 110 120 130 140 150
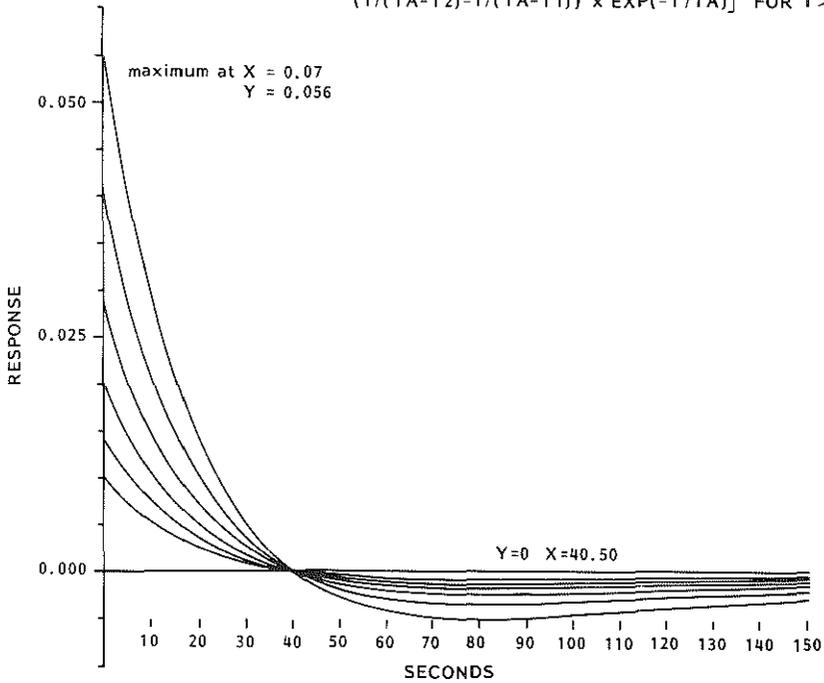
SECONDS

Fig. 4. Response of the second order model with adaptation, after an impulsive stimulation with amplitude factor 1, 1.4, 2, 2.8, 4 and 5.6. Cupular T_1=20 s; T_2=0.01 s; T_a= 100 s.

Table I. Estimated value of the response T_1 after an impulsive stimulation of the second order model with adaptation. The calculation is made by means of the decay method (fig.5).

Inserted in equation (6)			Response T_1	% of cupular T_1
T_a=100 s T_2=0.01 s	T_1=	10 s	7.8 s	78 %
		15	10.8	72
		20	13.8	69
		25	16.3	65
T_1=20 s T_2=0.01 s	T_a=	75 s	12.6 s	63 %
		100	13.8	69
		125	14.3	72
		150	14.7	74

```
V(T)=0                                                                    FOR T=≤0
V(T)=T1xT2x[(TA/(T1-T2)] x [(1/(TA-T1))          x EXP (-T/T1)-
                            (1/(TA-T2))          x EXP (-T/T2)+
                            (1//TA-T2)-1/(TA-T1)) x EXP (-T/TA)]  FOR T>0
```
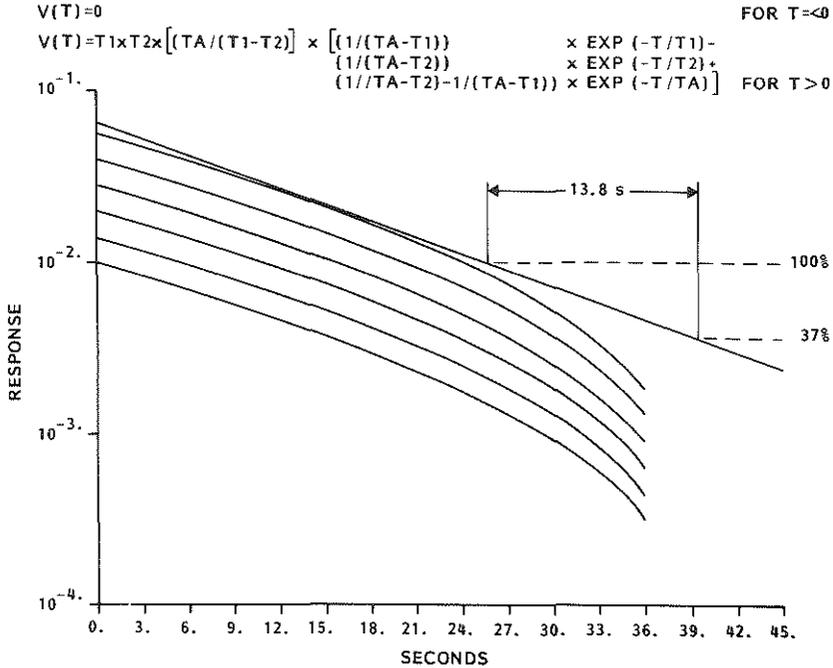
Fig. 5. Same as fig. 4, plotted on log-linear graph paper. The value of the response T_1, estimated by the decay method (a), is 13.8 s.

amplitude factors 1, 2 and 4. Again the threshold is chosen as 7.5% (0.0042 units) of the maximum response (0.056 units). In this figure the value of the response T_1 is estimated as 11.0 s. It should be noticed that the estimated value of the response T_1 is increased if a higher threshold is used (see table II).

Table II. Influence of the response threshold on the estimated value of the response T_1 in the cupulometric method.

Inserted T_1	Threshold	Response T_1	% of cupular T_1
cupular time constant T_1=20 seconds	0.0042 (7.5%)	11.0 seconds	55 %
	0.0084 (15 %)	13.4	67
	0.0125 (22.5%)	14.3	72
	0.0167 (30 %)	15.0	75

By using larger impulse amplitudes the estimated value of the response T_1 is decreased, as can be inferred from fig. 6.

Table III shows the effect of varying the values of the cupular T_1 and of the adaptation time constant on the estimated value of the response T_1. These variations have the same effect as described for table I.

$V(T) = 0$ FOR $T = <0$

$V(T) = T1 \times T2 \times \left[\{TA/(T1-T2)\} \times \left[\{1/(TA-T1)\} \right. \right.$ × EXP(-T/T1)-
$(1/(TA-T2))$ × EXP(-T/T2)+
$\left. \left. \{1/(TA-T2)-1/(TA-T1)\} \right] \right.$ × EXP(-T/TA)$\left. \right]$ FOR $T > 0$
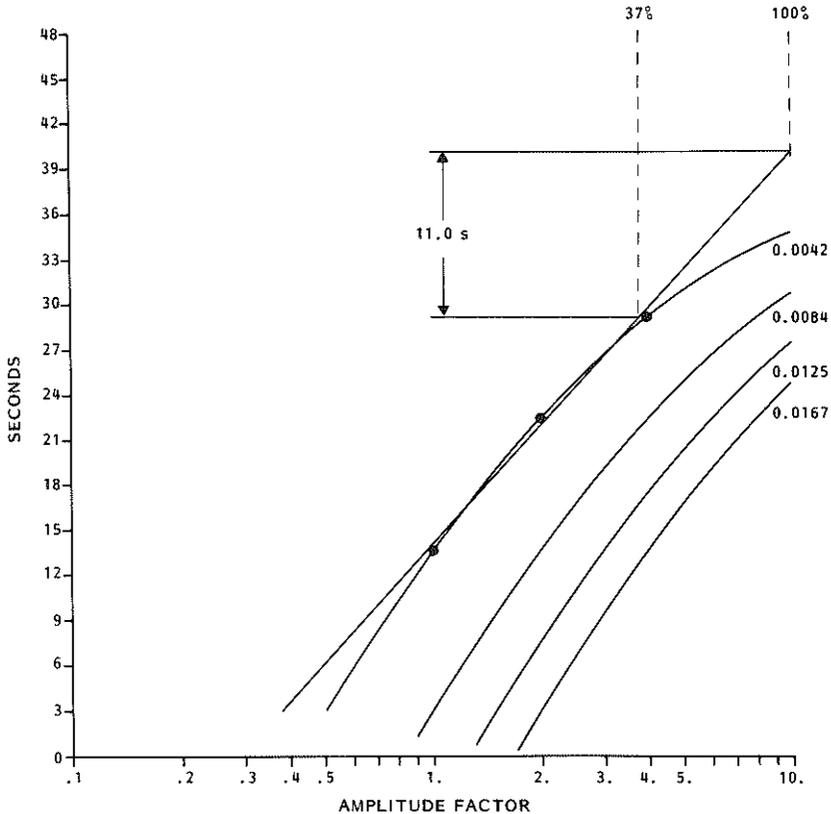
Fig. 6. Response duration until the threshold is reached, plot-ted against the logarithm of impulse amplitude. Second order model with adaptation, cupular T₁=20 s, T₂=0.01 s. Thresholds: 0.0042=7.5%; 0.0084=15%; 0.0125=22.5%; 0.167=30% of the maximum response. The value of the response T₁, estimated by the cupulometric method (b), is 11.0 s.

When a given set of cupular T_1, T_2 and T_a values is inserted in equation (6), all values of the response T_1 are lower in table III than in table I.

Conclusion: In the second order model with adaptation the value of the response T_1, estimated from the response curve after an impulsive stimulation, is lower than the value of the cupular T_1 which is inserted in the model. This reduction is more pronounced if:

- the value of the inserted T_1 is high;

- the value of the inserted T_a is low;
- the cupulometric method (b) is used instead of the decay method (a);
- in the cupulometric method, a low threshold is chosen for the determination of the duration of the response;
- in the cupulometric method, large stimulus amplitudes are chosen.

Table III. Estimated value of the response T_1 after an impulsive stimulation of the second order model with adaptation. The calculation is made by means of the cupulometric method (fig. 6).

Inserted in equation (6)			Response T_1	% of cupular T_1
T_a=100 s	T_2=0.01 s	T_1= 10 s 15 20 25	6.9 s 8.9 11.0 12.6	69 % 59 55 50
T_1=20 s	T_2=0.01 s	T_a= 75 s 100 125 150	9.9 s 11.0 11.9 12.8	50 % 55 60 64

DISCUSSION

The combination of the adaptation mechanism with the second order model leads to the presence of a prolonged period of reversed response. In clinical cupulometry this phenomenon is known as post-post-rotatory nystagmus (or after-nystagmus or secondary nystagmus or Nach-Nach Nystagmus). The maximum value of the reversed response and the moment at which this value is reached, are difficult to determine, as can be seen in fig. 4.
It is possible to read the moment at which the response reverses its direction, t_o, from the figure. It is determined by the value of the cupular T_1 and by that of the adaptation time constant T_a. Nevertheless, the estimation of the cupular T_1 and of the adaptation time constant T_a from a few marked data on the response curves after an impulsive stimulation is unreliable, because of the considerable interaction of the two time constants in the short time range in which the responses can be considered (see table III). *Malcolm and Melvill Jones* (1970) matched by eye the complete experimental response curves with their mathematical model and found a cupular T_1 of 21 s (S.E. $\pm$ 1.5 s) and a T_a of 82 s (S.E. $\pm$ 6.5 s). *Sills et al.* (1978) used a minicomputer to fit the experimental data. In their method of calculation they noted many imperfections. For two different impulse amplitudes they found a cupular T_1 of 16.6 and 18.2 s (μ= $\pm$ 5.5 s and $\pm$ 6.6 s), and a T_a of 99 s (μ= $\pm$ 44.0 s and $\pm$ 52.3 s). All in all, the response of the VOR-system to an impulsive stimulation will be influenced by the adaptation mechanism and will not be suitable for the single determination of the cupular T_1 and the time constant T_a.

In clinical cupulometry the duration of nystagmus for various impulse amplitudes is plotted against the logarithm of impulse amplitude. As a result of this theoretical study it is clear that the assumption of a threshold in slow phase eye velocity for determining the duration of the responses is preferable to the use of nystagmus as parameter. The implications of this statement are investigated in the following chapter *(Boumans et al., 198.b, chapter III)*.

CONCLUSIONS

Adaptation has a distinct effect on the response of the model of the human VOR-system after an impulsive stimulation. The effect of adaptation is to reduce the value of the response T_1, estimated from these responses, especially when the cupulometric method is used. The value of the response T_1 will be approximately 60% of the real value of the cupular time constant T_1.
The response curves of the system after impulsive stimulation do not seem suitable for the determination of the cupular time constant T_1 and the adaptation time constant T_a.

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CHAPTER III. INFLUENCE OF ADAPTATION UPON THE IMPULSIVE TIME
CONSTANT OF THE HUMAN VESTIBULO-OCULAR REFLEX (VOR) SYSTEM

II. EXPERIMENTAL INVESTIGATION

ABSTRACT. The response of the VOR-system was measured after a
start or stop in angular velocity around the vertical axis. All deter-
minations were carried out six times for 5 subjects. In a previous
study (Boumans et al., 1980, chapter I) the mean value of the response
T_1 was calculated from the slope of the decay of the slow phase eye
velocity (method a) and found to be 13.2 s (SD=1.4 s) for CW-stimula-
tion, and 12.8 s (SD=1.7 s) for CCW-stimulation. Using the cupulometric
method (b) with a fixed threshold for the slow phase eye velocity, these
values are 12.1 s (SD=2.0 s) and 11.2 s (SD=1.4 s) respectively. The
difference between the values calculated by method (a) and those cal-
culated by method (b) is in line with the theoretical predictions as
formulated in the previous chapter (Boumans et al., 198.a, chapter II).

INTRODUCTION

In a previous investigation (Boumans et al., 1980, chapter I) the
long time constant T_1 of the response of the VOR-system to an impulsive
stimulation was calculated from the slope of the decay of slow phase
eye velocity (SPV). This paper did not deal with the duration of the
nystagmus or the possible presence of after-nystagmus. On account of
the theoretical study (Boumans et al., 198.a) the experimental data
are reviewed in order to compare the results with the conclusions of
the theoretical study.
This was done in an attempt to answer the following questions:
(1)   Does the SPV, generated after an impulsive stimulation of various
        amplitudes in one direction, always change its sign at the same
        moment, t_o?
(2)   After what stimulus amplitude does the phenomenon of nystagmus
        reversal occur?
(3)   Does the value of the response T_1, calculated by the traditional
        cupulometric method using the duration of nystagmus as parameter,
        differ from the value of the response T_1, calculated by the same
        method using a fixed threshold of SPV as parameter?
(4)   Does the value of response T_1, calculated by the cupulometric
        method using a fixed threshold (method b), tend to be less than
        the value of response T_1 calculated by the decay method (a)?
(5)   Can we estimate the values of the cupular time constant T_1 and
        of the adaptation time constant T_a from the value of the experi-
        mental response T_1?

METHOD

The experimental data are the same as analysed in a previous
study (Boumans et al., 1980, chapter I). The reader is referred to this
paper for the description of the stimulus, the recording technique, the
subjects and the experimental procedure. The stimulus amplitude of 25 °/s

was included in this cupulometric evaluation while it was not used in the previous study because the response amplitudes were too small to determine the response T_1 from the slope of the decay. Data processing of all recordings was done by hand. Slow phase eye velocity was plotted on a linear scale and the duration of SPV for the various impulse amplitudes was determined, using a fixed threshold (7.5 °/s SPV). Cupulograms were made and the value of the response T_1 was calculated from the slope.

Attention was also given to the duration of the nystagmus, the phenomenon of nystagmus reversal and to the moment (t_0) at which the slow phase eye movement changed its direction.

RESULTS

Table I. Time at which SPV is zero, t_0, in s. The standard deviation is given in brackets. For the impulse amplitudes 25, 50 and 100 °/s: N>10. Nystagmus reversal is denoted by:

⊖ : *no reversal*

⊕̸ : *occasional reversal*

⊕ : *reversal always occurs*

Subject	CW Stimulation				CCW Stimulation			
	25°/s	50°/s	100°/s	140°/s	25°/s	50°/s	100°/s	140°/s
AS	35.8(9.7) ⊕	40.7(6.8) ⊕	40.8(2.0) ⊕	41.5 ⊕	51.8(6.2) ⊖	57.5(3.4) ⊕̸	50.0(2.4) ⊕	56.0 ⊕
MB	44.3(9.7) ⊖	49.8(12) ⊕̸	54.9(9.7) ⊕̸	55.0 ⊕	29.2(6.0) ⊕̸	33.8(6.5) ⊕	37.6(3.8) ⊕	38.5 ⊕
RM	39.0(7.9) ⊕	42.1(4.8) ⊕	44.2(2.5) ⊕	43.0(2.4) ⊕	41.4(4.4) ⊕	45.1(4.0) ⊕	47.2(3.1) ⊕	49.3(2.3) ⊕
HK	36.3(1.2) ⊕	37.0(1.8) ⊕	40.4(2.3) ⊕	38.8(1.7) ⊖	38.3(5.3) ⊕̸	39.6(2.1) ⊕̸	43.3(2.4) ⊕	41.0(1.8) ⊕
MR	30.0(2.2) ⊕	41.1(7.7) ⊕	39.1(2.7) ⊕	44.7(5.1) ⊕	52.0(2.4) ⊖	55.7(4.8) ⊖	46.5(3.8) ⊕̸	57.0(6.5) ⊕

The maximum slow phase eye velocity occurred between 4 and 6 s after the beginning of the impulse, for all subjects and all impulse amplitudes. The duration of the impulse itself was 2.5 s at most.

Table I shows the time (t_0) after the beginning of the impulse at which the SPV is zero. When nystagmus reversal does not occur, the value of t_0 is rather difficult to estimate and tends to be underestimated.

For subject HK the results are shown in fig. 1. The moment of SPV reversal appears to be the same for the various stimulus amplitudes, provided all stimuli are in one direction.

An example of the calculation of the value of the response T_1 by the traditional cupulometric method is shown in fig. 2.a: the duration of nystagmus is plotted against the logarithm of the impulse amplitude. Table II gives the values of the response T_1, calculated by this method, for all subjects. Only the impulse amplitudes 25, 50 and 100 °/s are used for this calculation, because saturation occurred at higher velocity.
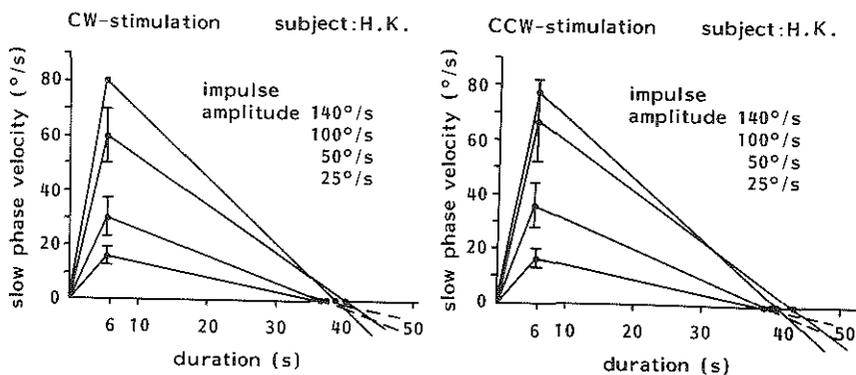
Fig. 1. Results in one subject. The beginning of the impulse, the maximum slow phase eye velocity and t_0 are connected by straight lines, not representing the actual SPV-profile. A dotted line represents an occasional occurrence of nystagmus reversal, a full line indicates that nystagmus reversal always occurs.
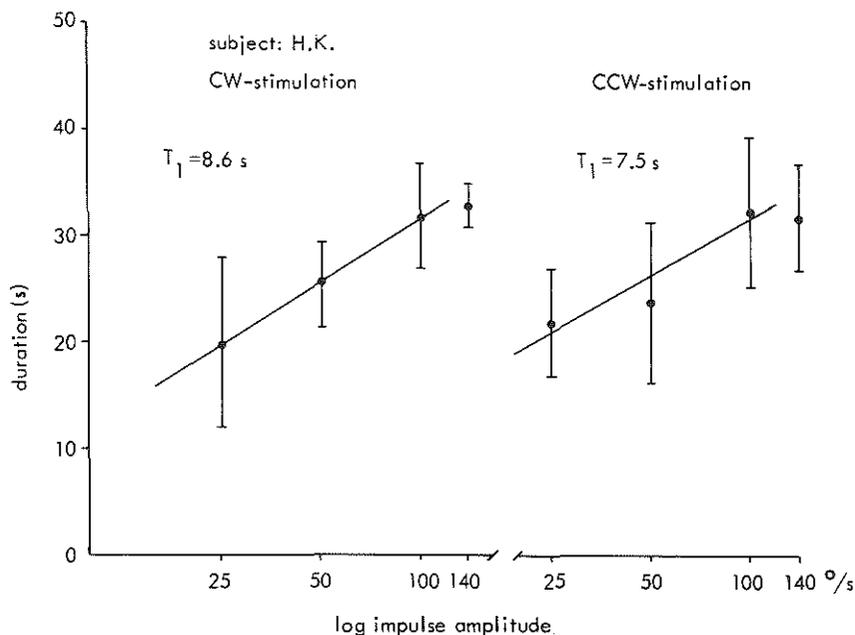
Fig. 2.a. Cupulogram of subject HK. The duration of nystagmus is employed as parameter. The bars represent 2 x SD.

Table II. Value of the response T_1, calculated by the traditional cupulometric method, using the presence of nystagmus as a threshold.

Subject	Response T_1 (CW)	Response T_1 (CCW)
AS	5.5 s	6 s
MB	13	6.5
RM	12	11
HK	8.5	7
MR	5.5	1

The mean value of the response T_1 is 8.9 s (SD= 3.5 s) after CW-stimulation and 6.3 s (SD=3.5 s) after CCW-stimulation; the range (1-13 s) is large.

subject: H.K.

CW-stimulation

$T_1 = 11.0$ s

CCW-stimulation

$T_1 = 10.4$ s
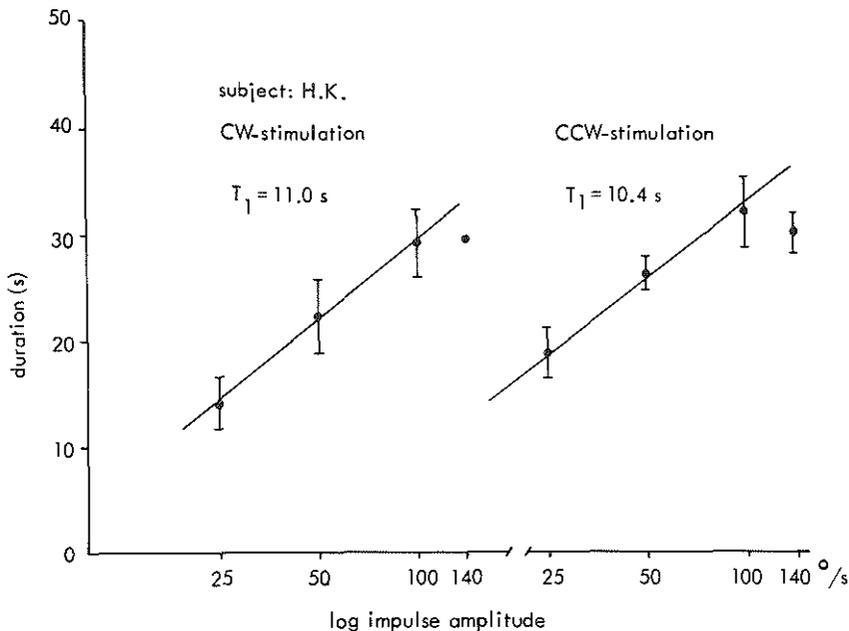
Fig. 2.b. Cupulogram of subject HK. The duration until a threshold of 7.5 °/s SPV is reached, is employed as parameter. The bars represent 2 x SD.

Fig. 2.b. shows the duration of SPV until the threshold of 7.5 °/s is reached, and it is for the same measurements in the same subject (method b). It is to be noted that higher estimates of the value of the response T_1 result from the latter procedure.

Table III. Value of response T_1, calculated by the cupulometric method and using 7.5 o/s SPV as a threshold.

Subject	Response T_1 (CW)	Response T_1 (CCW)
AS	9.5 s	9.5 s
MB	14.5	11.0
RM	12.0	12.3
HK	11.0	10.4
MR	13.5	13.0

In table III the values of the response T_1 are given for all subjects. After CW-stimulation the mean value is 12.1 s (SD=2.0 s), while after CCW-stimulation it is 11.2 s (SD=1.4 s).

Calculated by the decay method (a) the mean values of the response T_1 for CW- and CCW-stimulation are 13.2 s (SD=1.4 s) and 12.8 s (SD= 1.7 s) respectively *(Boumans et al., 1980, chapter I)*.

DISCUSSION

From a comparison of the theoretical considerations (chapter II) and the results of the measurements the following remarks can be made:
- In theory, for a second order model with adaptation and a given set of time constant values, all responses after an impulsive stimulation pass through zero at the same moment (t_0). The presence of an adaptive mechanism in the VOR-system is experimentally shown by the existence of nystagmus reversal (better SPV reversal). The moment of SPV reversal is found to be constant for each subject, provided all stimuli are in one direction (table I). For the subjects AS, MB and MR there is a distinct difference between the values of t_0 for CW- and CCW-stimulation. One has to bear in mind that in the region of t_0 the response curve is rather flat and thus even a slight directional asymmetry can explain the difference in t_0. This slight asymmetry does not appear to affect the value of the response T_1, calculated by the cupulometric method with a fixed threshold (method b), as it does in the traditional cupulometric method.
- In the theoretical study *(Boumans et al., 198.a, chapter II)* the necessity of the assumption of a threshold for SPV in the estimation of the value of the response T_1 was shown. The basis for measurement in traditional cupulometry is the presence of nystagmus (with a quick phase eye movement) and there is no fixed threshold. This leads to inconsistencies: the value of SPV above which nystagmus occurs differs from individual to individual; where there is nystagmus reversal this value of SPV can be very low, resulting in a low value of the response T_1 (compare fig. 2.a and 2.b). Intra-individual fluctuation of the nystagmus threshold leads to an additional problem *(Ranacher, 1977)*. Therefore it is concluded that the assumption of a fixed threshold for SPV is needed in cupulometric measurement.
- In a previous study *(Boumans et al., 1980, chapter I)* the value of the response T_1 was calculated from the impulse responses of the

VOR-system by the decay method (a), and found to be about 13 s. In the present study T_1 is calculated from the same data by the cupulometric method (b), and found to be about 11.7 s. These results bear out the theory as described in chapter II, where it is shown that when adaptation is present, method (b) gives a smaller apparent value of T_1 than method (a).

In the theoretical study the value of the response T_1 has been calculated for various values of the cupular T_1 and of the adaptive T_a.

Using the decay method (a) the value of the response T_1 is found to be 10.8-13.8 s for T_1=15-20 s and T_a=100 s; response T_1 is 12.6-13.8 s for T_1=20 s and T_a=75-100 s *(Boumans et al., 198.a, chapter II, table I)*.

Using the cupulometric method (b) the value of the response T_1 is found to be 11.0-12.6 s for T_1=20-25 s and T_a=100 s; response T_1 is 11.0-11.9 s for T_1=20 s and T_a=100-125 s *(Boumans et al., 198.a, chapter II, table III)*.

A comparison of the experimental results with the theoretical calculations suggests that in reality the cupular time constant T_1 is about 20 s, while the adaptation time constant T_a is 100-125 s. However, as pointed out in the discussion of the theoretical paper, this estimation is unreliable and in fact other combinations of values for cupular T_1 and T_a are also possible.

CONCLUSION

Adaptation has a distinct effect on cupulometric measurement. This investigation seems to justify the mathematical models describing the mechanical function of the semicircular canal and the adaptation mechanism *(Boumans et al., 198.a, chapter II)*. The effect of adaptation is to reduce the value of the response T_1 calculated from the nystagmographic responses after an impulsive stimulation, especially when the cupulometric method (b) is used. The calculated value will be approximately 60% of the value of the cupular time constant T_1. It is recommended that a fixed threshold value for SPV should be employed in cupulometric measurement, rather than the presence of nystagmus.

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SECTION II: SINUSOIDAL STIMULATION OF THE HUMAN VOR-SYSTEM

CHAPTER IV: FREQUENCY RESPONSE OF THE HUMAN VESTIBULO-OCULAR
REFLEX (VOR) SYSTEM AT LOW FREQUENCIES: THE EFFECT OF ADAPTATION

I. THEORETICAL STUDY

ABSTRACT. From the mathematical model of the human VOR-system
the frequency response has been calculated for harmonic sinusoidal
acceleration. The addition of an adaptation term to the second order
model, describing the cupular behaviour, results in considerable changes
in the response characteristics in the low frequency region. An attempt
has been made to quantify the influence of the cupular time constant
T_1 and the adaptation time constant T_a on the amplitude and phase charac-
teristics of the transfer function, which represents the human VOR-
system. The results of this theoretical study will be employed in the
following chapter *(Boumans et al., 198.d, chapter V)*.

INTRODUCTION

In the prevailing mathematical model of the transfer function of
the human vestibular system the second order model of the cupular be-
haviour is modified by the addition of an adaptation term. The frequency
response of the pure second order model to harmonic sinusoidal accelera-
tion is extensively described in the literature. A recent summary can
be found in Mammalian Vestibular Physiology *(Wilson and Melvill Jones,*
1979). By the addition of the adaptation term to the second order model
the frequency response of the vestibular system will be changed in the
low frequency region. The effect of a short term adaptation mechanism
has been shown experimentally, for example, in the frequency response
of peripheral neurons innervating the semicircular canals of the squirrel
monkey *(Fernandez and Goldberg,* 1971), and in the phase characteristic
for the vestibular sensation of rotation in man *(Rodenburg et al.,*
1977). Neither the effect of adaptation on the response of the human
VOR-system to sinusoidal oscillation, nor the effect of varying the
values of the cupular time constant T_1 and of the adaptation time con-
stant T_a have previously been calculated. It is thus the aim of the
present study
(1)   to describe qualitatively how the frequency characteristic of the
       second order model is altered when an adaptation term is added
       and
(2)   to show quantitatively how the amplitude ratio and the phase re-
       lationship depend on the cupular time constant T_1 and the adap-
       tation time constant T_a.
The reader is referred to the APPENDIX for a comprehensive description
of the derivation of the equations used.

METHOD AND RESULTS

According to the *second order model* the linear transfer function
relating the cupular displacement, θ_c, to the applied angular head ve-
locity, $\dot{\theta}_h$, is (in Laplace notation):

$$H(s) = \frac{\theta_c(s)}{\theta_h(s)} = \frac{T_1 \cdot T_2 \; s}{(T_1 s + 1)(T_2 s + 1)} \tag{1}$$

where T_1=the long time constant of cupular restoration;
    T_2=the short time constant.
In the real time domain the amplitude ratio is:

$$\alpha = \frac{\omega \; T_1 \cdot T_2}{\sqrt{(\omega T_1)^2 + 1} \; \cdot \; \sqrt{(\omega T_2)^2 + 1}} \tag{2}$$

where ω=freq. in radians/s; $\omega = 2\pi x$freq.
The phase relationship is:

$$\phi = \frac{\pi}{2} - \arctan(\omega T_1) - \arctan(\omega T_2) \tag{3}$$
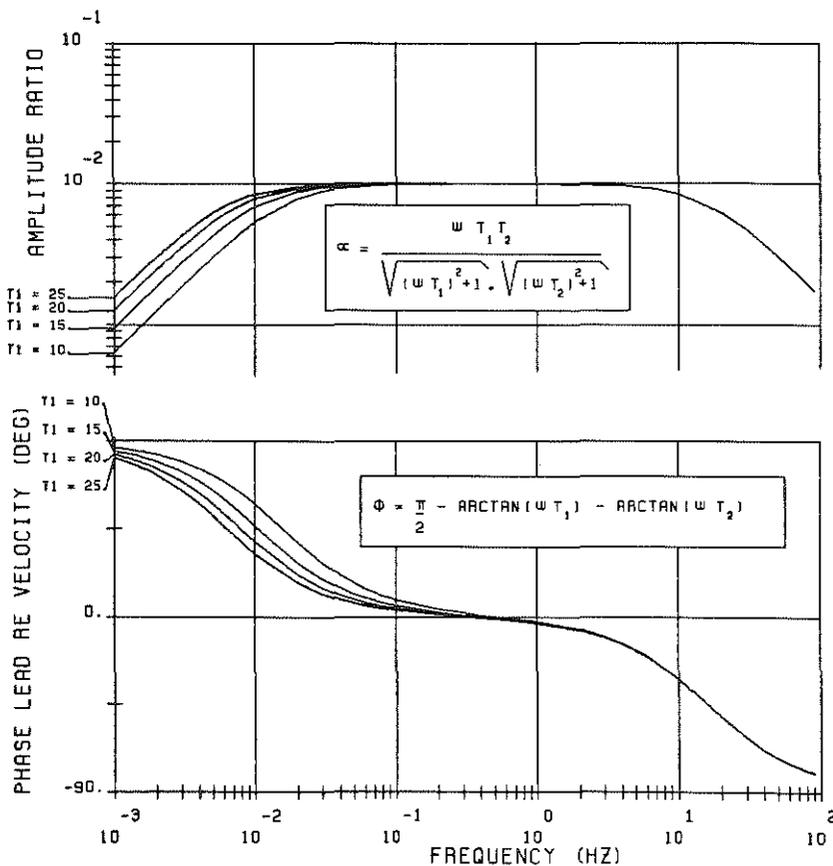
Fig. 1. Bode plot (re velocity) for the dynamic frequency response
of the cupula-endolymph system, based on equation (1). Variable value
for T_1; fixed value of T_2=0.01 s.

In fig. 1 the amplitude ratio and the phase of the cupular displacement
(re velocity) are plotted as functions of the stimulus frequency. The
so-called asymptotic upper cut-off frequency is determined by the value
of T_2, the lower cut-off frequency by that of T_1. The values of T_1 and
T_2 in fig. 1 are chosen close to the values found in the literature.

The amplitude equation shown in the figure:

$$\alpha = \frac{\omega^2\, T_1\, T_2\, T_R}{\sqrt{(\omega T_1)^2 + 1}\, \cdot\, \sqrt{(\omega T_2)^2 + 1}\, \cdot\, \sqrt{(\omega T_R)^2 + 1}}$$

The phase equation shown in the figure:

$$\Phi = \pi - \mathrm{ARCTAN}(\omega T_1) - \mathrm{ARCTAN}(\omega T_2) - \mathrm{ARCTAN}(\omega T_R)$$
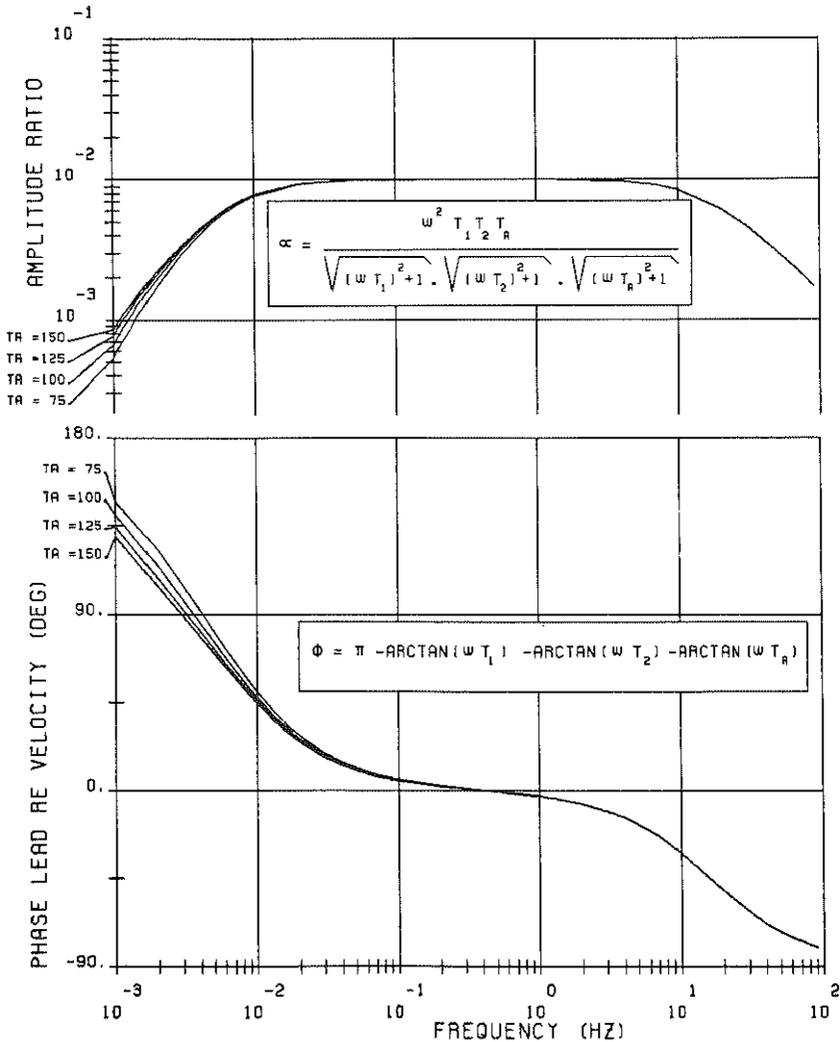
*Fig. 2. Bode plot (re velocity) for the dynamic frequency respon-
se of the human VOR-system, based on equation (5). Variable value for
T_a; fixed value of T_1=20 s; fixed value of T_2=0.01 s.*

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In the high frequency region the amplitude ratio decreases and there
is a phase lag of up to 90 degrees. The amplitude ratio again decreases
at low frequencies, whereas the cupular displacement shows a phase lead
of up to 90 degrees.

The transfer function of the *adaptation mechanism*, according to
Young and Oman (1969) and *Melvill Jones* (1970), is described by:

$$H_a(s) = \frac{\dot{\theta}_e(s)}{\theta_c(s)} = \frac{T_a s}{T_a s + 1} \tag{4}$$

where $\dot{\theta}_e$ = angular eye velocity.

Adding the *adaptation model* to the *second order model* results in the
following over-all transfer function for the VOR-system:

$$H(s) = \frac{\dot{\theta}_e(s)}{\theta_h(s)} = \frac{T_1 \cdot T_2 \cdot T_a s^2}{(T_1 s + 1)(T_2 s + 1)(T_a s + 1)} \tag{5}$$

The amplitude ratio is:

$$\alpha = \frac{\omega^2 \quad T_1 \cdot T_2 \cdot T_a}{\sqrt{(\omega T_1)^2 + 1} \cdot \sqrt{(\omega T_2)^2 + 1} \cdot \sqrt{(\omega T_a)^2 + 1}} \tag{6}$$

The phase is:

$$\phi = \pi - \arctan(\omega T_1) - \arctan(\omega T_2) - \arctan(\omega T_a) \tag{7}$$

Fig. 2 shows the dynamic frequency response of the VOR-system as given
by equation (5). It must be noted that both amplitude ratio and phase
are expressed with respect to the angular velocity of the stimulus.
When fig. 1 is compared with fig. 2 it is seen that the curves differ
at low frequencies: in fig. 2 the amplitude ratio decreases more steep-
ly and the phase lead becomes more than 90 degrees.

The quantitative effect of varying the values of the cupular time
constant T_1 and the adaptation time constant T_a on the amplitude ratio
and the phase relationship is studied in Bode plots of the low frequency
response derived from equation (5).

In fig. 3 the *amplitude characteristics* for various values of T_1
are shown. The amplitude ratios at frequencies of 0.01 Hz and of
0.001 Hz have been calculated as shown in table I: at the very low
frequency of 0.001 Hz the effect of varying the value of T_1 is even
greater than at 0.01 Hz. The result of varying the time constant T_a
is shown in fig. 4. The amplitude ratios for various values of T_a at
a frequency of 0.001 Hz have been calculated as shown on the right
hand side of table I: the effect appears to be less than that of
varying the value of T_1 at the same frequency.

The *phase characteristics* for the various values of T_1 and T_a,
as derived from equation (5), are shown in fig. 5 and fig. 6, respec-
tively. The effect of varying the value of T_1 on the phase is greatest
in the region of 0.01 Hz, whereas the maximum effect of varying the
value of T_a lies just above 0.001 Hz. At this latter frequency, varia-
tion of T_1 no longer has noticeable effect on the phase while it still
has considerable effect on the amplitude ratio. The values of the phase
lead (re velocity) are shown in table II, and range from 42 to 67
degrees at 0.01 Hz (based on a variable value of T_1), and from 130
to 148 degrees at 0.001 Hz (based on a variable value of T_a).

Table I. Values of the amplitude ratio (α) for the human VOR-system in harmonic sinusoidal acceleration at 2 different frequencies, based on equation (5).

Inserted in equation (5)		α
$\omega=2\pi f$	$T_1=10$ s	53.10^{-4}
$f=0.01$ Hz	15	68
$T_2=0.01$ s	20	77
$T_a=100$ s	25	83
$\omega=2\pi f$	$T_1=10$ s	33.10^{-5}
$f=0.001$ Hz	15	50
$T_2=0.01$ s	20	66
$T_a=100$ s	25	83

Inserted in equation (5)		α
$\omega=2\pi f$	$T_a=75$ s	53.10^{-5}
$f=0.001$ Hz	100	66
$T_1=20$ s	125	77
$T_2=0.01$ s	150	86

Table II. Values of the phase lead (with respect to velocity) for the human VOR-system in harmonic sinusoidal acceleration at 2 different frequencies, based on equation (5).

Inserted in equation (5)		Phase (deg)	Inserted in equation (5)		Phase (deg)
$\omega=2\pi f$	$T_1=10$s	67	$\omega=2\pi f$	$T_a=75$s	148
$f=0.01$ Hz	15	56	$f=0.001$ Hz	100	141
$T_2=0.01$ s	20	48	$T_1=20$ s	125	135
$T_a=100$ s	25	42	$T_2=0.01$ s	150	130

$$\alpha = \frac{\omega^2 \, T_1 \, T_2 \, T_a}{\sqrt{(\omega T_1)^2 + 1} \cdot \sqrt{(\omega T_2)^2 + 1} \cdot \sqrt{(\omega T_a)^2 + 1}}$$
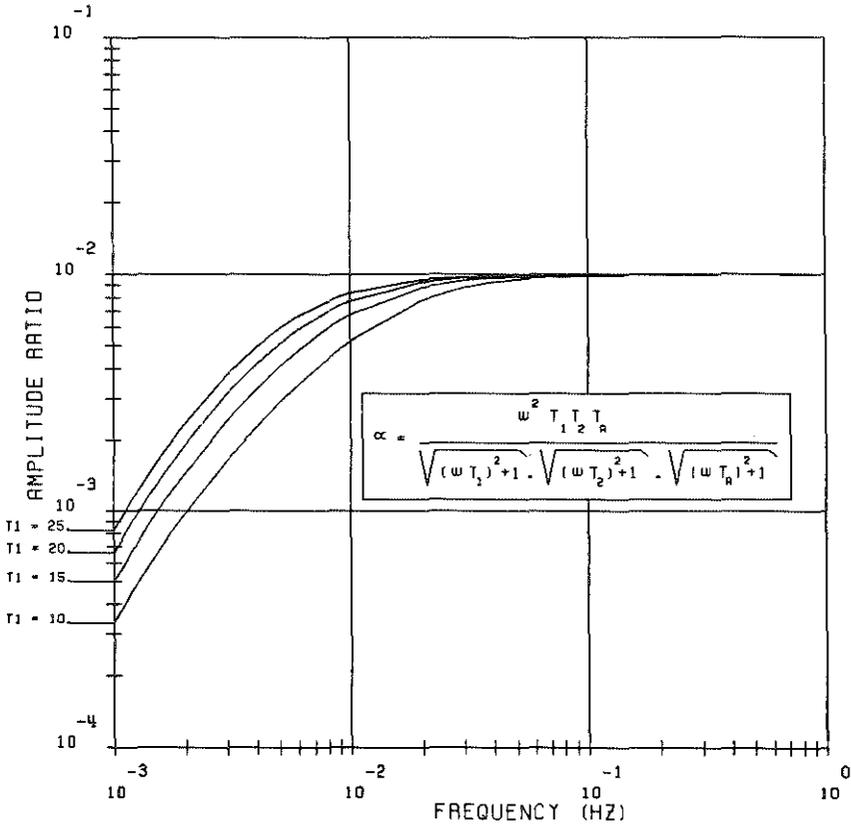
Fig. 3. Amplitude characteristic (re velocity) of the low frequency response derived from equation (5). Variable value for T_1; fixed value of T_a=100 s. The values of the amplitude ratio at frequencies of 0.01 Hz and 0.001 Hz can be found in table I.

$$\alpha = \frac{\omega^2 T_1 T_2 T_R}{\sqrt{(\omega T_1)^2+1} \cdot \sqrt{(\omega T_2)^2+1} \cdot \sqrt{(\omega T_R)^2+1}}$$
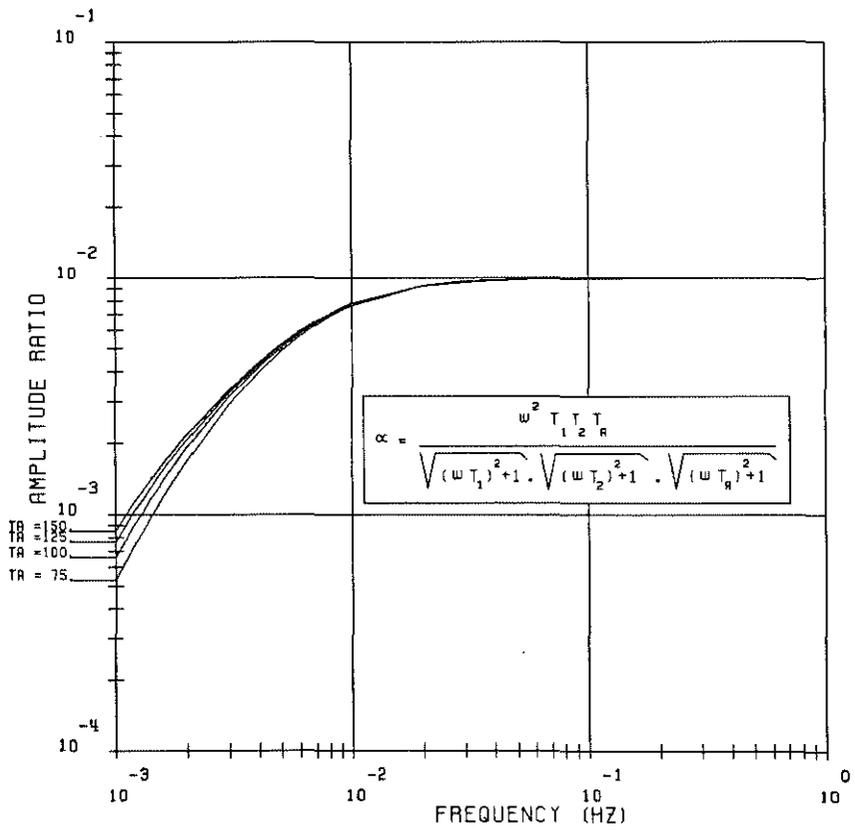
Fig. 4. Same as fig. 3. Variable value for T_a; fixed value of $T_1=20$ s. The values of the amplitude ratio at a frequency of 0.001 Hz can be found in table I.
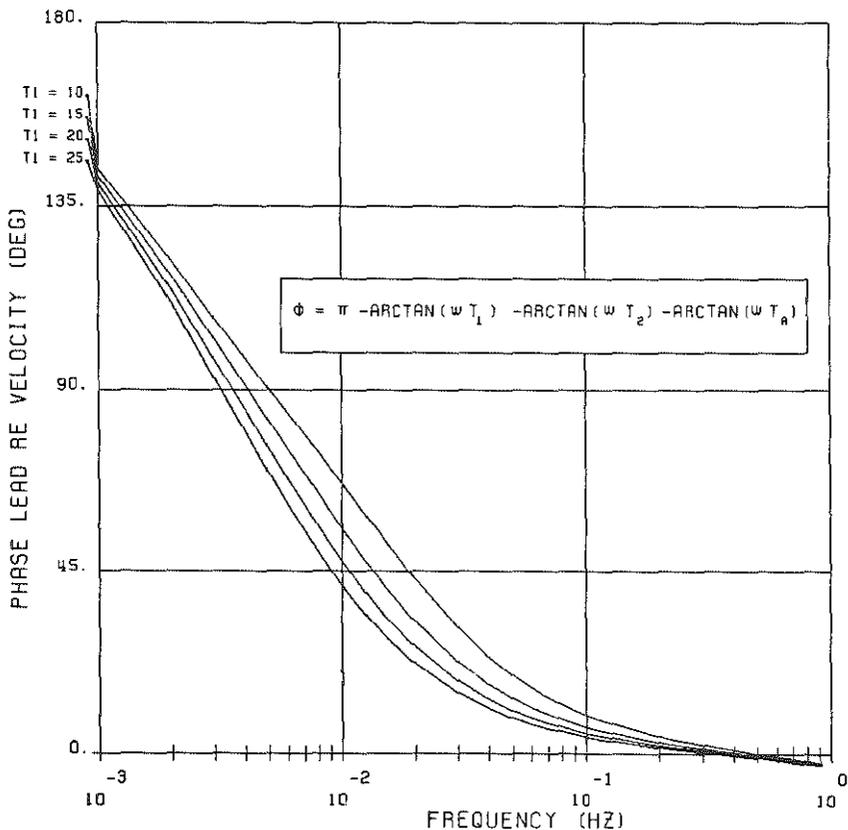
Fig. 5. Phase characteristic (re velocity) of the low frequency response derived from equation(5). Variable value for T_1; fixed value of T_a=100 s. The values of the phase lead at a frequency of 0.01 Hz can be found in table II.

The graph shows labels:

$T_1 = 10.$
$T_1 = 15.$
$T_1 = 20.$
$T_1 = 25.$

$$\Phi = \pi - ARCTAN(\omega T_1) - ARCTAN(\omega T_2) - ARCTAN(\omega T_A)$$

Y-axis: PHASE LEAD RE VELOCITY (DEG), with values 180., 135., 90., 45., 0.

X-axis: FREQUENCY (HZ), with values 10^{-3}, 10^{-2}, 10^{-1}, 10^{0}

DISCUSSION

The addition of the adaptation term to the second order model of the cupula-endolymph system alters the over-all transfer function which represents the VOR-system (from equation(1) to equation(5)), in such a way that there is a distinct change in the low frequency region.

In the *amplitude characteristic* the amplitude ratio decreases by 12 dB per octave at very low frequencies (fig. 2), instead of by 6 dB per octave as in the second order model (fig. 1). One might expect to be able to estimate the value of T_a from the amplitude characteristic

in this very low frequency region. However, the value of the amplitude
ratio at very low frequencies is determined to a greater degree by the
value of the cupular time constant T_1 than by that of the adaptation
time constant T_a (see table I).

For this reason the determination of the amplitude characteristic
of the VOR-system is not a suitable method for the calculation of
the time constant T_a. At a frequency of 0.01 Hz the influence of adap-
tation is rather small, so that the amplitude ratio or gain in the
VOR-system at that frequency will to a great extent be determined by
the value of the cupular T_1, and, conversely, the value of T_1 could here
be determined from the amplitude ratio.

The situation appears to be different with respect to the *phase
characteristic* of the frequency response derived from equation (5).
In the first place, a phase lead of more than 90 degrees can occur when
the adaptation term is added to the second order model. Further the
effect of varying the value of the cupular T_1 will largely be seen in
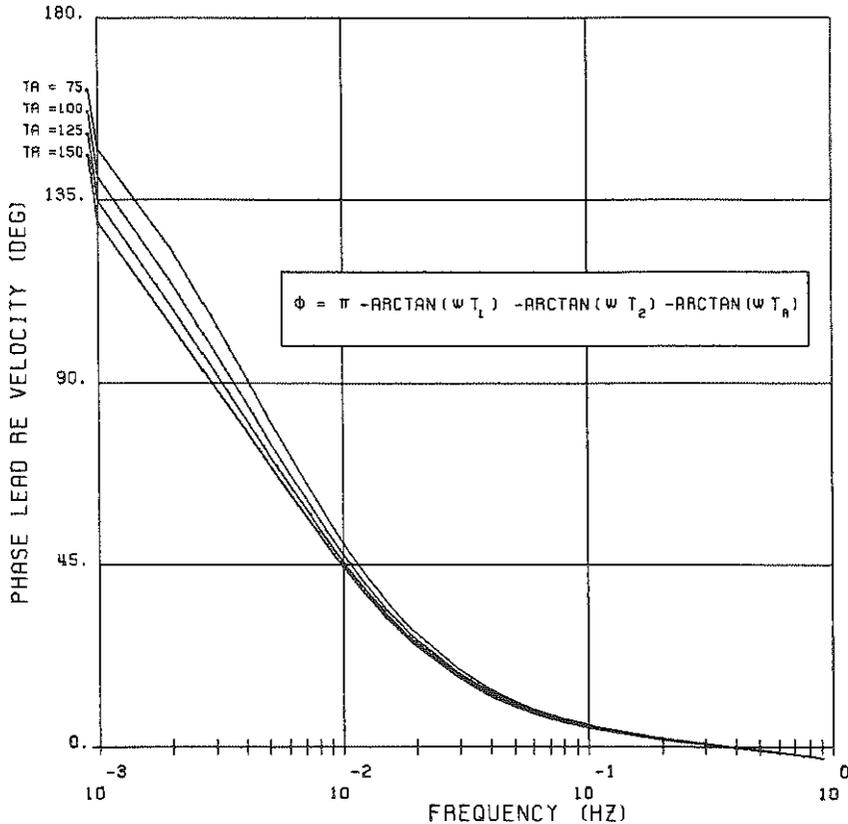
Fig. 6. Same as fig. 5. Variable value for T_a; fixed value of
$T_1=20$ s. The values of the phase lead at a frequency of 0.001 Hz can
be found in table II.

the frequency region around 0.01 Hz, whereas it is the value of T_a that
determines the phase lead at very low frequencies. This phenomenon will
be used in the following chapter (chapter V) where we shall estimate
the values of the cupular time constant T_1 and the adaptation time
constant T_a from experimental data, obtained by harmonic sinusoidal
acceleration of the human VOR-system.

CONCLUSION

At low frequencies adaptation has a distinct effect on the trans-
fer function which represents the human VOR-system. The amplitude ratio
in the frequency region around 0.01 Hz is largely determined by the value
of the cupular time constant T_1, whereas at very low frequencies the
values of both T_1 and T_a have an influence. On the other hand, the phase
lead at 0.01 Hz is largely determined by the value of T_1, whereas at
0.001 Hz it is largely determined by that of T_a. Hence the experimental
determination of the phase characteristic of the human VOR-system could
be used as a way of calculating the cupular T_1 and the adaptation time
constant T_a.

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CHAPTER V: FREQUENCY RESPONSE OF THE HUMAN VESTIBULO-OCULAR RE-
FLEX (VOR) SYSTEM AT LOW FREQUENCIES: THE EFFECT OF ADAPTATION

II. EXPERIMENTAL INVESTIGATION

ABSTRACT. The frequency response of the human VOR-system was in-
vestigated by determining its amplitude and phase characteristics. The
angular head velocity and the resulting angular eye velocity were mea-
sured in 7 healthy subjects using a rotation room. Rotations about the
vertical axis were carried out at frequencies ranging from 0.0025 Hz
to 0.1 Hz; peak head velocity was 50 ^{o}/s. From the experimental data
the gain and the phase relationship were calculated. The results appear
to be in agreement with the frequency response of the theoretical trans-
fer function which represents the VOR-system. This is based on a second
order differential equation for cupular behaviour, modified by an adap-
tation term *(Bowmans et al., 198.c, chapter IV).* According to the ex-
perimental phase characteristic the cupular restoration time constant
T_1 was 16.6 s, and the adaptation time constant was 114 s. Linearity
of the VOR-system, both for amplitude and phase, was demonstrated at
frequencies of 0.05 Hz and 0.005 Hz.

INTRODUCTION

In the investigation of the human VOR-system the frequency response
to harmonic sinusoidal stimulation has been studied at middle and high
frequencies.
Niven and Hixon (1961) used a steady-state sinusoidal rotation
with frequencies ranging from 0.02 to 0.20 Hz and a constant peak angular
acceleration of 40 ^{o}/s^2. They determined the phase characteristic in
6 subjects. From the phase at 0.02 Hz the long time constant T_1 was
calculated. Its value varied from 6.5 s to 10.2 s and, measured in one
particular subject, appeared to be dependent on the stimulus amplitude.
Later the dependence of the phase shift on the stimulus amplitude
was further investigated *(Hixon and Niven,* 1962). For that purpose peak
angular accelerations of 10 to 80 ^{o}/s2 were used. Linearity was demon-
strated above a frequency of 0.04 Hz. At frequencies of 0.04 and 0.02 Hz
the phase lead (re stimulus velocity) became greater as higher peak
acceleration values were used.
Meiry (1966) determined the amplitude and the phase characteris-
tics for frequencies between 0.028 Hz and 2.0 Hz in 7 subjects. The
gain (ratio of the peak slow phase eye velocity (SPV) to the peak stimu-
lus velocity) was 0.43 Hz at all frequencies. The phase lead (re velocity)
varied from 35 degrees at 0.028 Hz to -26 degrees at 2.0 Hz.
Benson (1970) investigated the transfer function of the VOR-system
in the frequency range from 0.01 Hz to 2.0 Hz, in 9 subjects. The peak
angular acceleration was 30 ^{o}/s2. At frequencies between 0.05 Hz and
0.5 Hz the gain was 0.7; below 0.05 Hz the gain decreased, whereas above
0.5 Hz it increased. The phase shift varied from 53 degrees at 0.01 Hz
to zero degrees at 2.0 Hz. In a supplementary investigation in 6 subjects
the phase remained at zero degrees up to 5 Hz.
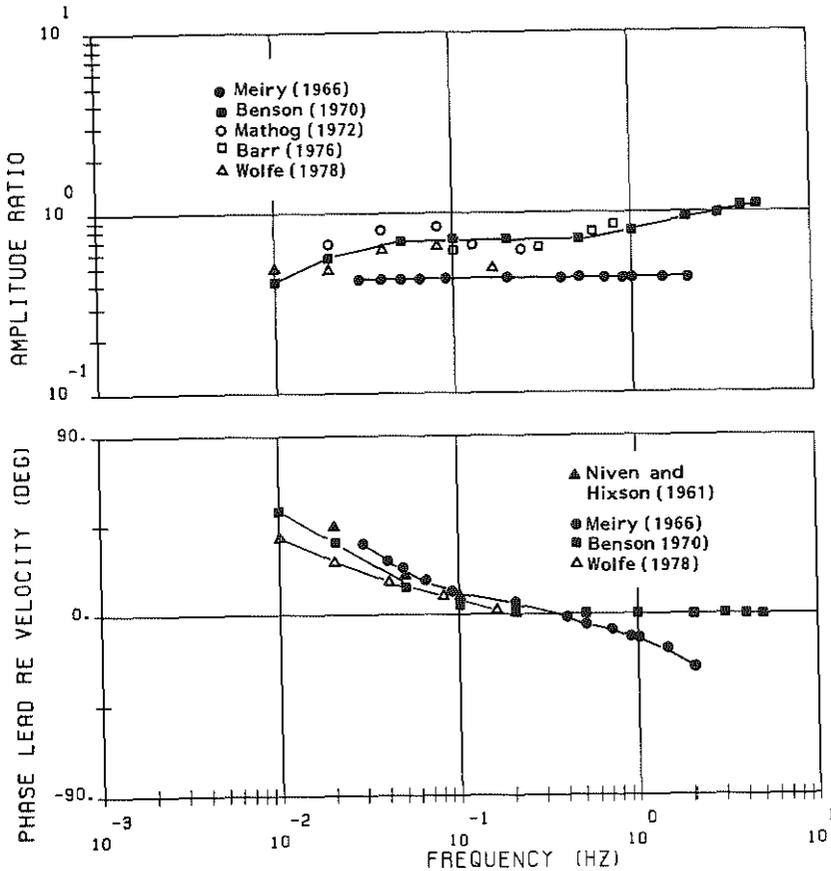
Fig. 1. Bode plot (re velocity) of the frequency response of the human VOR-system, based on data found in the literature.

Mathog (1972) determined the amplitude characteristic in the frequency range from 0.02 Hz to 0.24 Hz. In one group of 16 subjects a constant peak angular acceleration of 0.4 rad/s2 was used. The gain varied from 0.55 to 0.80 and was almost independent of the frequency. In another group of 6 subjects the peak acceleration was varied from 0.2 to 0.6 rad/s2. Linearity was observed above a frequency of 0.03 Hz. Reworking the data in that paper it is possible to see that the non-linearity found below 0.03 Hz was due to saturation: at a frequency of 0.02 Hz linearity can be shown up to a stimulus peak velocity of 180 °/s.
Barr et al.(1976) found a gain increase from 0.62 at 0.1 Hz to 0.83 at 0.8 Hz.
Wolfe et al.(1978) investigated the canal function by harmonic sinusoidal

acceleration (0.01 Hz–0.16 Hz) in 50 normal subjects. Peak stimulus ve-
locity was held constant at 50 °/s. The gain was found to be 0.5 at
frequencies of 0.01 Hz and 0.02 Hz, 0.64 at 0.04 Hz and 0.08 Hz, and
0.5 at a frequency of 0.16 Hz. The phase ranged from 39 degrees at
0.01 Hz to 3.5 degrees at 0.16 Hz.

A summary of the data found in the literature is given in fig. 1:
a.   The gain of the VOR-system appears to be fairly constant in the
     mid-frequency region (0.02 Hz–0.1 Hz). At high frequencies an
     increase of the gain is sometimes observed; a decrease is not
     reported. In the low frequency region a decrease of the gain was
     found by *Benson*.
b.   The phase relationship of the SPV with respect to stimulus velocity
     shows a phase lead at low frequencies. Below 0.01 Hz data are
     lacking. Above 0.3 Hz *Meiry* observed a phase lag, whereas *Benson*
     did not find a phase shift at frequencies of up to 5 Hz.
c.   The findings in the literature are inconsistent with respect to
     linearity.

According to the theoretical considerations in chapter IV of this
thesis, it is at low frequencies that the effect of adaptation on the
vestibular transfer function can be expected, where it can result in
a phase lead of more than 90 degrees. This effect has been demonstrated
in Scarpa's ganglion of primates *(Fernandez and Goldberg,* 1971) and in
a psychophysical study in man *(Rodenburg,* 1977).

In the vestibulo-ocular reflex system of normal subjects the in-
fluence of adaptation on sinusoidal stimulation has not been investi-
gated systematically. *Wolfe et al.* (1978a) found, when comparing patients
with healthy subjects, that there were differences in the phase and/or
the directional preponderance in the low frequency region (0.01 Hz–
0.04 Hz), which revealed deficits in the peripheral function. *Mathog*
(1972) also found the greatest divergence between normal and patholo-
gical cases at low frequencies.

The purpose of the present study is to investigate the transfer
function of the normal human VOR-system at low frequencies. The inter-
pretation of the experimental data is based on the results obtained
from the theoretical study in chapter IV of this thesis and is directed
towards an analysis of the performance of the cupula-endolymph system
and the adaptation mechanism.

METHOD

a. Stimulus
The stimulus was a sinusoidal angular acceleration administered
by a rotation room with a hydrostatic bearing. An electrohydraulic servo-
motor drives the room via a belt. The motor is controlled by a small
electrical signal from a function generator. A technical description
of the rotation room has been given by *Teerhuis et al.* (1979). The fol-
lowing frequencies were used: 0.0025, 0.005, 0.01, 0.02, 0.05 and 0.1 Hz;
the peak angular velocity was 50 °/s at all frequencies. The resulting
movement of the room has been analysed by the Fourier method: the fre-
quency of motion of the room deviated by less than 5% from the adjusted
frequency.

I

DATA ACQUISITION

II

EX-FILE ⟶ NYSTAN ⟶ OUT-FILE

INTERACTIVE ANALYSIS PROGRAM

III

OUT-FILE → PREPO → FFT → FIT →
frequency :
phase :
amplitude :
DC-shift :

SINEWAVE FITTING PROGRAM
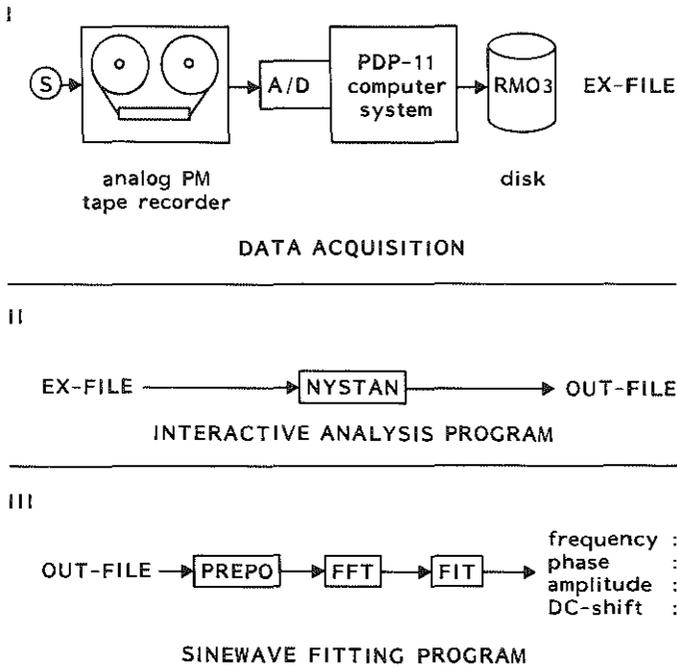
Fig. 2. Outline of the analytical procedure.

b. Subjects and procedure

 A group of 7 healthy males with no apparent defects in hearing
and equilibrium was used as subjects. The cab enclosure was light-proof
and no ambient lighting was provided during the entire run. The subjects
were allowed to adapt to the dark until the corneo-retinal potential
had stabilized (about 15 minutes). They sat in a chair with the vertex
at the centre of rotation and the head fixed in a holder. The nystagmus
recordings were made with open eyes and for the maintenance of optimal
nystagmus response the subjects were kept alert by listening to re-
corded performances of an entertainer.

 Each test sequence was measured five times in each subject. One
or more weeks was allowed to elapse between the test sequences to mini-
mize possible effects of habituation. The test sequences were started
alternately at high and low frequency. To exclude initial transient
phenomena the recording of the eye movement was started up to 200 s
after the start of the stimulus.

 For the investigation of linearity various amplitudes at frequen-
cies of 0.05 Hz and 0.005 Hz were used in 3 subjects, always starting
with the lowest amplitude. Each test sequence was measured five times
in each subject.

```
NO

      332              333  334      335         336          337
      41.4             42.4 42.7     43.1        43.6         44.3
      -6.5             -7.3 -6.6     -9.0        -10.0        -12.9

                                                      CHOOSE>

T                                                                    FAS


41              42              43              44              4
S
```
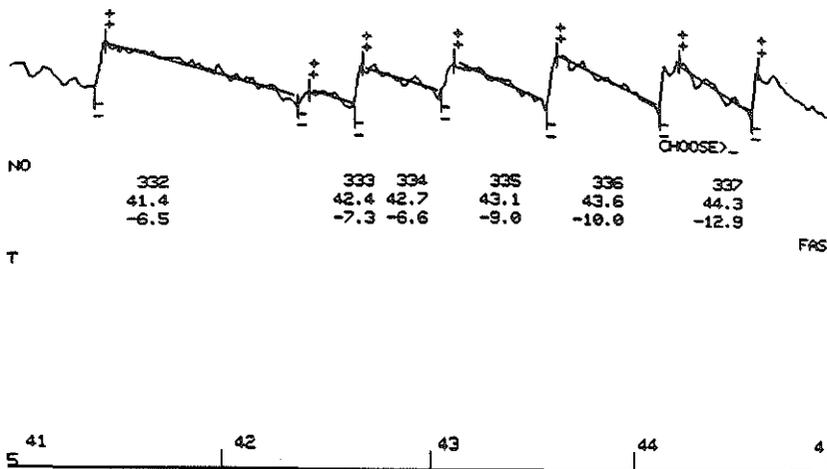
Fig. 3. Example of the interactive analysis program. The slow phase eye velocity decreases from -6.5°/s at 41.4 s to -12.9°/s at 44.3 s.
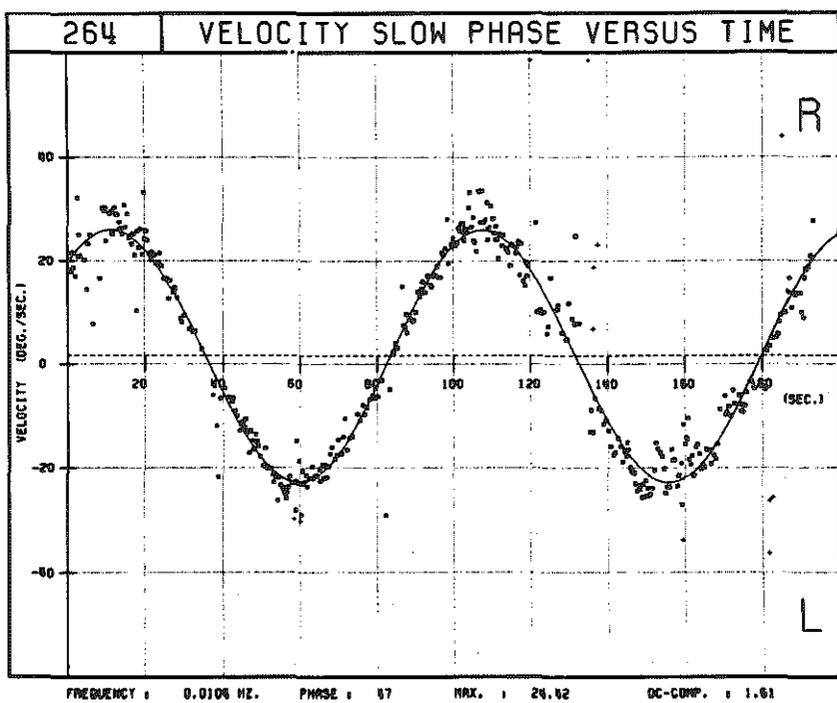

Fig. 4. Result of the sinewave fitting program in an experiment where a stimulus frequency of 0.0105 Hz was used.

Horizontal eye position was recorded by DC-electro-oculography
using bi-temporal electrodes, taped near the outer canthi of the eyes.
The signals were amplified by a Tektronix TM 502 amplifier with the fol-
lowing characteristics: common mode rejection, 100 dB; input impedance,
100 MΩ; gain 5x10^3; frequency response, DC-100 Hz. The DC offset of the
EOG-signal was compensated for by a digital automatic device for over-
range correction *(Maas et al.,* 1982). The amplified signals were recor-
ded on magnetic tape by a Bell & Howell 4010 recorder with AD 8 PCM
system (4 channels; frequency response, DC-70 Hz). The room position
was also recorded.

d. Data processing

An outline of the analytical procedure is shown in fig. 2. After
analog to digital signal conversion the mean calibration was used to
analyse the intervening data. The interactive analysis program was ob-
tained from Dr *P.Huijgen* of Nijmegen University (1979). An example of
the processing is given in fig. 3.

A sinewave fitting program was especially developed by the Auto-
matic Signal Processing Department of the Medical Faculty. The data
from the analysis program were preprocessed removing, for example, ex-
treme data from the period of time where the slow phase eye velocity
changed its direction. A first rough fit was performed by the Fast Fou-
rier Transform (FFT) method, giving the basic frequency and an indication
of the phase. Thereafter a final fit was obtained by the least squares
method and the result was plotted as is shown in fig. 4.

RESULTS

*Table I. Mean peak slow phase eye velocity in °/s, using 50 °/s
as peak stimulus velocity for all frequencies in 7 subjects. The mean;
(standard deviation); number of experiments are listed.*

FREQUENCY (Hz)	LB	MB	MR	LV	RM	AS	HK	MEAN (N=7)
0.0025	7.8(1.9)3	8(0.4)3	11(1.8)3	11(2.1)4	6(2.3)3	8(1.7)4	9(2.0)4	8.7(1.8)
0.005	9 (4.7)4	15(2.5)9	18(5.0)9	16(2.2)5	10(1.2)10	15(2.9)5	13(1.3)4	14 (3.5)
0.01	13 (1.5)3	23(3.5)5	29(7.3)4	22(3.2)5	18(2.1)5	24(3.1)5	24(3.0)4	22 (5.0)
0.02	16 (0.9)3	30(3.7)4	28(9.2)3	30(2.3)5	26(4.5)5	27(1.6)5	33(3.8)4	27 (5.8)
0.05	21 (4.8)4	32(5.8)9	38(5.2)10	32(3.2)5	31(2.7)10	34(2.8)5	35(3.7)4	32 (5.4)
0.1	27 (1.1)2	35(1.6)3	40(4.1)4	33(3.7)4	32(1.6)4	30(1.5)5	38(4.8)3	34 (4.5)

In table I the mean peak SPV is given for all frequencies in each
subject. The mean values for all subjects (N=7) are listed in the right
hand side of the table, where it can be seen that the gain decreases
at low frequencies.

The phase lead of SPV is given in the same way in table II, which
shows that it exceeds 90 degrees at the very low frequency of 0.0025 Hz.
Such a phase lead could not be demonstrated in the subjects MR, RM and
AS, so an additional experiment was performed in these subjects, using
frequencies of 0.0025 Hz and 0.0010 Hz (see table III). Thus it was poss-

ible to demonstrate the effect of adaptation in all subjects, provided a sufficiently low frequency was used for the stimulus.

Table II. Mean phase of slow phase eye velocity with respect to stimulus velocity, using 50 º/s as peak stimulus velocity for all frequencies in 7 subjects. The mean; (standard deviation) are listed.

Frequency (Hz)	LB	MB	MR	LV	RM	AS	HK	MEAN (N=7)
0.0025	101(10)	147(8)	69(10)	109(7)	90(4)	91(4)	118(8)	104(25)
0.005	70(4)	85(9)	77(6)	73(7)	83(10)	82(3)	93(10)	80(8)
0.01	48(8)	50(5)	52(8)	42(7)	50(5)	50(3)	52(8)	49(3)
0.02	29(8)	27(5)	24(5)	26(5)	30(4)	32(4)	34(5)	29(3)
0.05	21(3)	21(8)	16(9)	15(10)	16(7)	13(2)	15(8)	17(3)
0.1	7(4)	6(4)	3(13)	9(11)	3(12)	9(6)	4(8)	6(3)

Linearity at low frequencies was investigated by measuring the frequency response of the VOR-system in 3 subjects. The results are presented in fig. 5 : the amplitude ratio and the phase lead appear to be independent of the stimulus amplitude at the low frequencies of 0.05 Hz and 0.005 Hz.

Table III. Phase lead of slow phase eye velocity with respect to stimulus velocity, in 3 subjects. Peak stimulus velocity was 100 º/s for both frequencies.

Frequency (Hz)	MR	RM	AS
0.0010	100	137	116
0.0025	82	90	88

Curve fitting of the experimental data

In order to estimate the values of the cupular time constant T_1 and the adaptation time constant T_a of the human VOR-system, points representing the mean values of the gain and the phase for all subjects were superimposed on the Bode plots which were described in chapter IV *(Boumans et al., 198.c)*.

a.   Amplitude characteristic

In fig. 6 the normalized values of the mean peak SPV for all subjects (in table I) are superimposed on the amplitude characteristic of the second order model with an adaptation term. The plot is the same as fig. 3 in chapter IV, where the value of the cupular time constant T_1 has been varied from 10-25 s. The value of the cupular T_1 can be estimated from the experimental data in fig. 6 as lying between 15 and 20 seconds.

The amplitude characteristic with a variable value for the adaptation time constant T_a (as in fig. 4 in chapter IV) is however not

suitable for the estimation of T_a, as was explained in chapter IV, and hence it is here omitted.
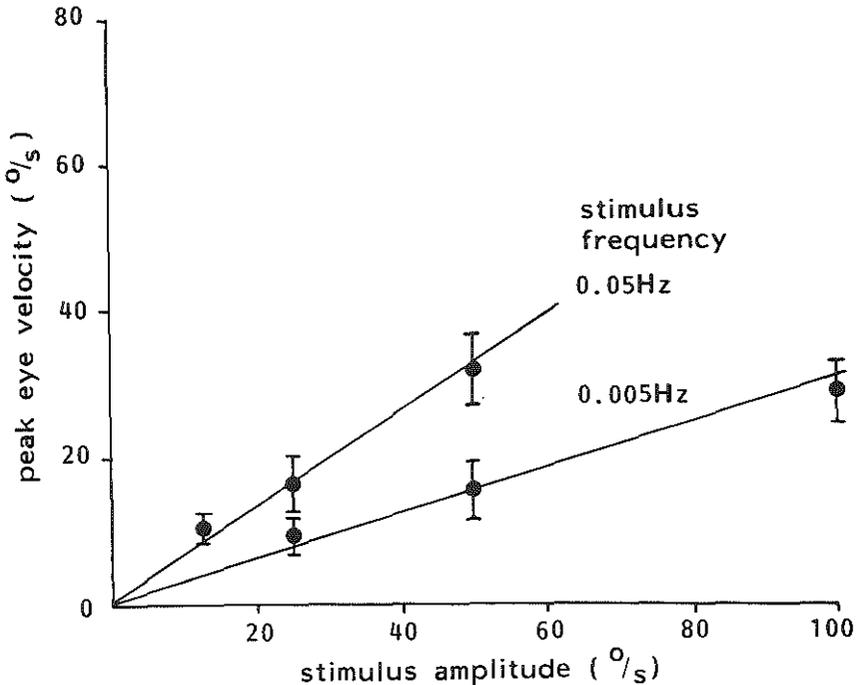

Fig. 5a. For legend: see fig. 5b.

b.   Phase characteristic
    The mean values of the phase lead (re velocity) for all subjects (given in table II) are superimposed on the phase characteristic of the second order model with adaptation (fig. 7). The curves plotted are comparable with those in fig. 5 and fig. 6 in chapter IV. According to fig. 7A the value of the cupular T_1 estimated from the experimental data again lies between 15 and 20 s.
    For that reason 17.5 s is chosen as the fixed value for T_1 in fig. 7B. In these phase characteristics the value of the adaptation time constant T_a has been varied from 75-150 s ·(compare with fig. 6 in chapter IV, where the fixed value of the cupular time constant T_1=20 s). The value of T_a estimated from the experimental data lies between 100 and

125 seconds. Finally the least squares method was used to fit the theoretical phase characteristic to the experimental data on the phase lead in all subjects, giving a cupular time constant T_1 of 16.6 s and an adaptation time constant of 114 s (fig. 8).
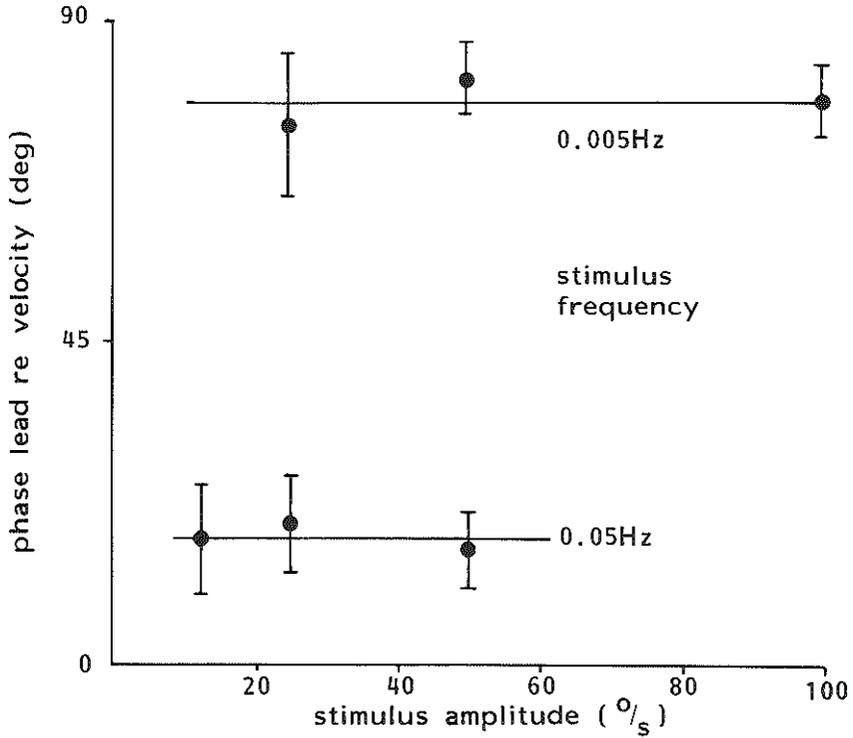

Fig. 5b.

Fig. 5. For several stimulus amplitudes the mean SPV (°/s) and the mean phase (deg) of SPV are calculated for stimulus frequencies of 0.05 Hz and 0.005 Hz. Bar is 2xSD.

$$\alpha = \frac{\omega^2 \, T_1 \, T_2 \, T_R}{\sqrt{(\omega T_1)^2+1} \cdot \sqrt{(\omega T_2)^2+1} \cdot \sqrt{(\omega T_R)^2+1}}$$
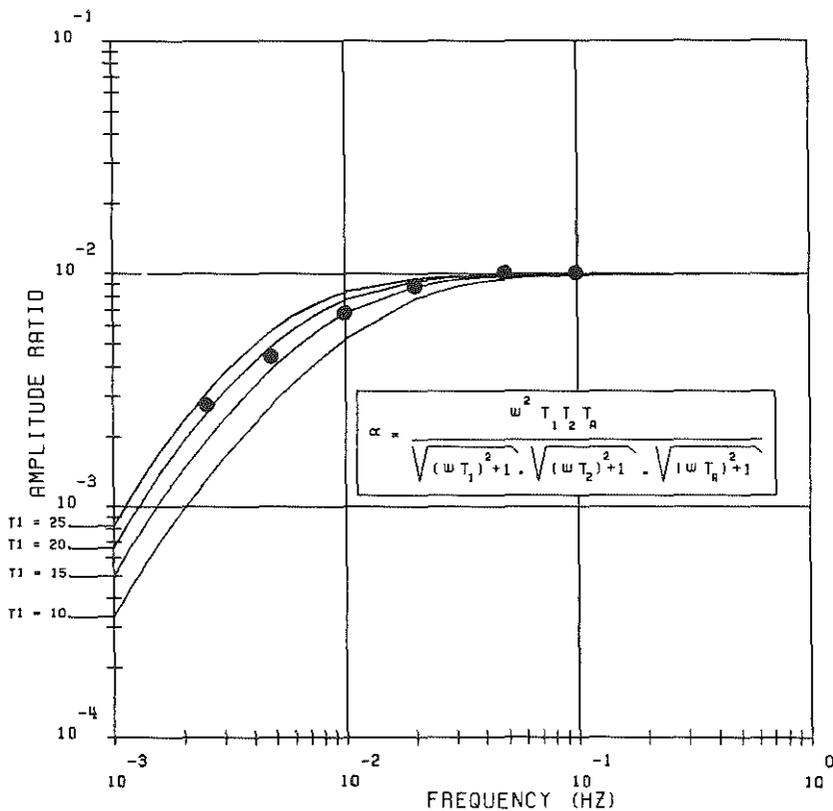
Fig. 6. Amplitude characteristic (re velocity) of the low frequency response of the theoretical transfer function of the VOR-system (see chapter IV, fig 3). Variable value for T1; fixed value of T_a=100 s. The normalized mean values of the mean peak SPV for all subjects are inserted in the figure. The estimated value of the cupular T1 lies between 15 and 20 s.

DISCUSSION

There are several difficulties in the determination of the frequency response of the human VOR-system at low frequencies. First, as it takes a long time to measure the sinusoidal oscillation (the experiment being made even longer by the need to eliminate the initial transient phenomenon), there is the problem of keeping the subject alert. It is known that the gain will to a considerable extent be decreased by drowsiness. Furthermore the gain in any case decreases of its own accord at low frequencies. For these reasons we used greater stimulus amplitudes for the additional investigation of the phase at a frequency of 0.001 Hz (table III).

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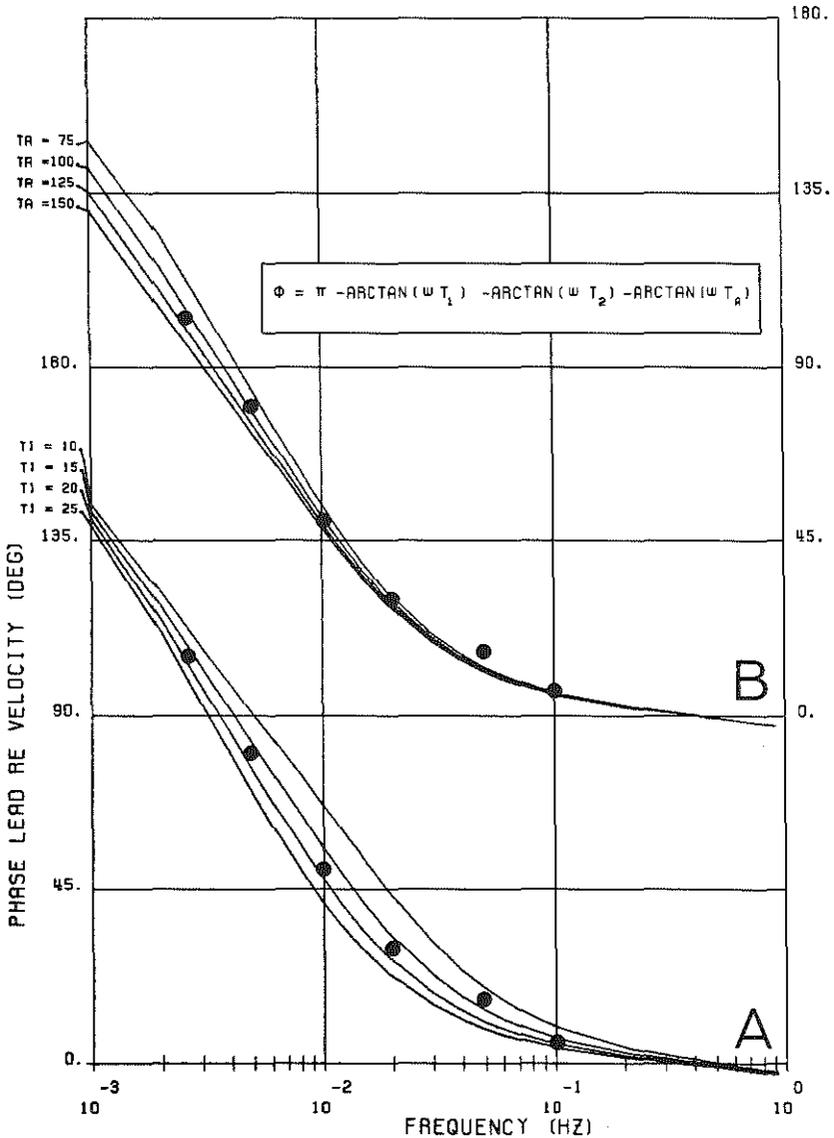
Fig. 7. Phase characteristic (re velocity) of the low freqyency response of the theoretical transfer function of the VOR-system (see chapter IV, fig. 5 and fig. 6).
A.   Lower set of curves. Variable value for T1; fixed value of Ta=100 s.
B.   Upper set of curves. Variable value for Ta; fixed value of T1=17.5 s.
The mean values of the mean phase lead for all subjects are inserted in the figure. In (A): the estimated value of the cupular time constant T1 lies between 15 and 20 s. In (B): the estimated value of the adaptation time constant Ta lies between 100 and 125 s.

Another difficulty is that small values of SPV (<3-5 °/s) are not registered in the interactive analysis program *(Huijgen,* 1979), which means that the sinewave fitting program will give too large a value for the calculated peak SPV when the experimental values of SPV are low.

The fundamental unsuitability of the amplitude characteristic for the estimation of the adaptation time constant T_a was discussed in the theoretical chapter IV. Furthermore the value of the experimental gain at low frequencies is influenced by variable factors such as drowsiness as mentioned above. Thus it was not feasible to use the amplitude characteristic to estimate the adaptation time constant T_a of the human VOR-system.

$$\Phi = \pi - \text{ARCTAN}(\omega T_1) - \text{ARCTAN}(\omega T_2) - \text{ARCTAN}(\omega T_a)$$

$$T_1 = 16.6 \text{ s}$$
$$T_a = 114 \text{ s}$$
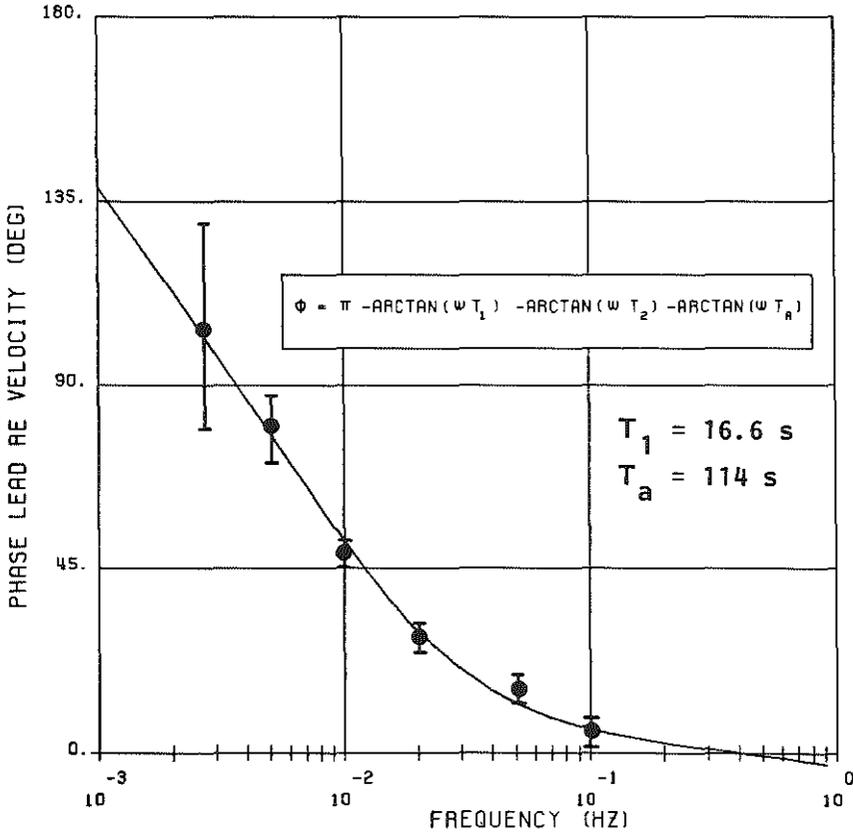
Fig. 8. The points show at each frequency the mean value for all subjects of the mean phase lead (Bar is 2xSD). The curve shows the phase characteristic, derived from the theoretical transfer function of the VOR-system, which best fits the experimental points. For this curve T_1=16.6 s, T_2=0.01 s and T_a=114 s.

As predicted in chapter IV the phase lead of the human VOR-system becomes more than 90 degrees in the low frequency region. However, the

phase lead in that region differs strongly among the subjects: the mean value of the phase lead at 0.0025 Hz is 69 degrees in subject MR, whereas it is 147 degrees in subject MB (table II).

With such great differences between normal subjects it will be difficult to use the frequency response curve of the VOR-system as a means of differentiating between healthy and sick individuals.

Linearity of the human VOR-system was also investigated at low frequencies. Even at the very low frequency of 0.005 Hz, where the effect of adaptation has been demonstrated, the system appears to be linear with respect to both the amplitude and the phase (fig. 5). Thus adaptation does not seem to disturb linearity.

CONCLUSION

The gain of the human VOR-system decreases in the low frequency region, whereas the phase lead becomes more than 90 degrees. The experimental data are in close agreement with the theoretical predictions derived from the second order model of cupular behaviour, when an adaptation mechanism is included. When the experimental data are fitted to the phase characteristic of the transfer function, the cupular time constant T_1 is found to be 16.6 s, while the adaptation time constant $Ta=114$ s.

Linearity with respect to the amplitude and the phase is demonstrated at frequencies of 0.05 Hz and 0.005 Hz.

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SECTION III

CHAPTER VI: RESPONSE OF THE HUMAN VESTIBULO-OCULAR REFLEX (VOR)
SYSTEM TO CONSTANT ANGULAR ACCELERATION

I. THEORETICAL STUDY

ABSTRACT. The response of the human VOR-system to a constant angu-
lar acceleration is calculated using a second order model with an adap-
tation term. After first reaching a maximum the peracceleratory response
declines. When the stimulus duration is long the decay is mainly governed
by the adaptation time constant T_a, which enables this time constant
to be reliably estimated. In the postacceleratory period of constant
velocity there is a reversal in response. The magnitude and the time
course of the per- and postacceleratory response are calculated for
various values of the cupular time constant T_1, the adaptation time
constant T_a and the stimulus duration, thus enabling their influence
to be assessed.

INTRODUCTION

In previous studies we investigated the response of the human
VOR-system to impulsive *(Boumans et al.,* 198.a and b, chapters II and
III) and to sinusoidal *(Boumans et al.,* 198.c and d, chapters IV and V)
stimulation. The experimental data appeared to be consistent with the
theoretical prediction that the response of the VOR-system is influenced
by both the cupular time constant T_1 and the adaptation time constant
T_a. Due to their interaction a quantitative investigation of the adap-
tation mechanism proved difficult.

In the case of a prolonged constant angular acceleration the de-
flection of the cupula will follow an exponential time course, reaching
a constant angular displacement after a period of about 4-5 times the
cupular time constant T_1. From that point, the response of the VOR-sys-
tem will be influenced by the adapatation mechanism alone. The use of
a constant acceleration for the stimulus therefore appears to be a suita-
ble method of investigating the adaptation mechanism. However, the
literature shows that in the few cases where this method has been em-
ployed there is great variety both in the parameters considered and in
the final results. A survey of the data found in the literature will
be given in the following chapter *(Boumans et al.,* 198.f, chapter VII).
Here we shall study the response of the mathematical model of the VOR-
system to a constant input and investigate which parameters can be
used to estimate the time constants of the system. The reader is referred
to the APPENDIX for a comprehensive description of the derivation of the
equations used.

METHOD AND RESULTS

Steinhausen (1933) put forward the torsion pendulum model of the
semicircular canals, where the relation between the cupular displace-
ment and the input acceleration is given by a second order differential
equation.

The response of the system to a step input is:

$$\theta_C(t) = 0 \qquad\qquad\qquad\qquad\qquad \text{for } t = < 0$$

$$\theta_C(t) = T_1 \cdot T_2 \ \left(1 - \frac{T_1}{T_1 - T_2} \cdot e^{-t/T_1} + \frac{T_2}{T_1 - T_2} \cdot e^{-t/T_2}\right) \ \text{for } t > 0 \qquad (1)$$

where θ_C=angular deflection of the cupula;
$\qquad$ T_1=long time constant of cupular restoration;
$\qquad$ T_2=short time constant ≈ 0.01 s.
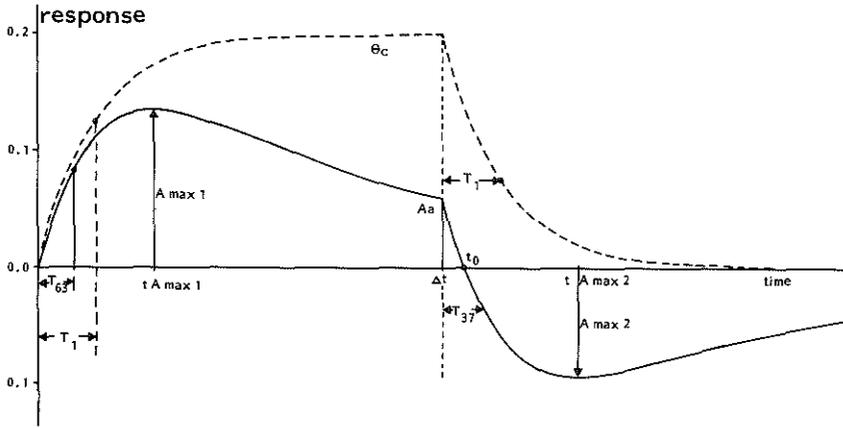
Fig. 1. Dotted line: time course of the cupular displacement θ_c, according to the second order model; constant angular acceleration during the period of time Δt. Solid line: time course of the VOR-response, according to the second order model with adaptation; constant angular acceleration during the period of time Δt. Amax1 is the peracceleratory response maximum, reached at the time t Amax1; Aa is the response value at the end of the stimulus period (Δt). Amax2 is the response minimum, reached at the time t Amax2 during the period of constant velocity. t_0 is the time at which response reversal occurs. $T_{63} = T_r$: time constant of the peracceleratory response rise. $T_{37} = T_f$: time constant of the post-acceleratory response fall.

According to this model the time course of the angular deflection of the cupula after the onset of a constant acceleration increases exponentially to reach a maximum after a period of 4-5 times the cupular time constant T_1; it then remains constant at a level determined by the product $T_1 \times T_2$ and by the stimulus amplitude. When the acceleration ceases and the velocity again becomes constant, the cupula will recover its resting position because of its elastic restoring force. In fig. 1 the dotted line represents the cupular behaviour given by equation (1). If the vestibular response (sensation and nystagmus) reflects cupular displacement, then the response should reach a maximum, then remain constant. During the period of constant velocity that follows, the vestibular response should decline to zero in a similar way. However, it is well known that during prolonged stimulation the peracceleratory

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response may gradually decline after reaching a maximum, and that a reversal in response often appears during the following period of constant velocity. An example of the time course of the vestibular response is given in fig. 1 (solid line).

The deviation of the vestibular response from the second order behaviour has lead to the assumption that there is an adaptation mechanism. Its transfer function (H_a) has been derived by *Young and Oman* (1969) and *Malcolm and Melvill Jones* (1970); in Laplace notation it is:

$$H_a(s) = \frac{\dot{\theta}_e(s)}{\theta_c(s)} = \frac{T_a s}{T_a s + 1} \tag{2}$$

where $\dot{\theta}_e$=angular eye velocity. The gain of the adaptation mechanism is assumed to be unity.

Combining the second order model with the adaptation mechanism, the over-all transfer function of the VOR-system is:

$$H(s) = \frac{\dot{\theta}_e(s)}{\ddot{\theta}_h(s)} = \frac{T_1 \cdot T_2 \cdot T_a s}{(T_1 s + 1)(T_2 s + 1)(T_a s + 1)} \tag{3}$$

where $\ddot{\theta}_h$=angular head acceleration.

The response of this function to a velocity ramp (constant angular acceleration) with a duration Δt will be, in the real time domain:

$$\dot{\theta}_e(t) = o \qquad\qquad\qquad\qquad \text{for } t = < o$$

$$\dot{\theta}_e(t) = \frac{T_1 \cdot T_2 \cdot T_a}{T_1 - T_2} \left\{ \frac{T_1}{T_a - T_1} (1 - e^{-t/T_1}) - \frac{T_2}{T_a - T_2} (1 - e^{-t/T_2}) \right.$$

$$\left. + \left(\frac{T_a}{T_a - T_2} - \frac{T_a}{T_a - T_1}\right)(1 - e^{-t/T_a}) \right\} \qquad \text{for } o < t < \Delta t \tag{4}$$

In the postacceleratory period of constant angular velocity, the response is :

$$\dot{\theta}_e(t) = \frac{T_1 \cdot T_2 \cdot T_a}{T_1 - T_2} \left\{ \frac{T_1}{T_a - T_1} (e^{-(t-\Delta t)/T_1} - e^{-t/T_1}) \right.$$

$$- \frac{T_2}{T_a - T_2} (e^{-(t-\Delta t)/T_2} - e^{-t/T_2}) \tag{5}$$

$$\left. + \left(\frac{T_a}{T_a - T_2} - \frac{T_a}{T_a - T_1}\right)(e^{-(t-\Delta t)/T_a} - e^{-t/T_a}) \right\} \text{ for } t > \Delta t$$

The equations (4) and (5) have been programmed and multiplied by various acceleration amplitudes. The values of the cupular T_1, T_2 and of T_a are chosen as 20, 0.01 and 100 s respectively, which are close to the values found in the literature. The response curves, simulating the slow phase eye velocity (SPV), are shown in fig. 2. In this example the peracceleratory response reaches a maximum (Amax1) at 40 s, after which it declines. The value (Aa) of the response at the end of the acceleration period (Δt) is 46% of Amax1. In the postacceleratory period the response rapidly declines and crosses the zero level 7.5 s after the end of the acceleration. Subsequently a secondary response appears, reaching its minimum value (Amax2) 47 seconds after the end of the acceleration. Then the response gradually returns to zero.
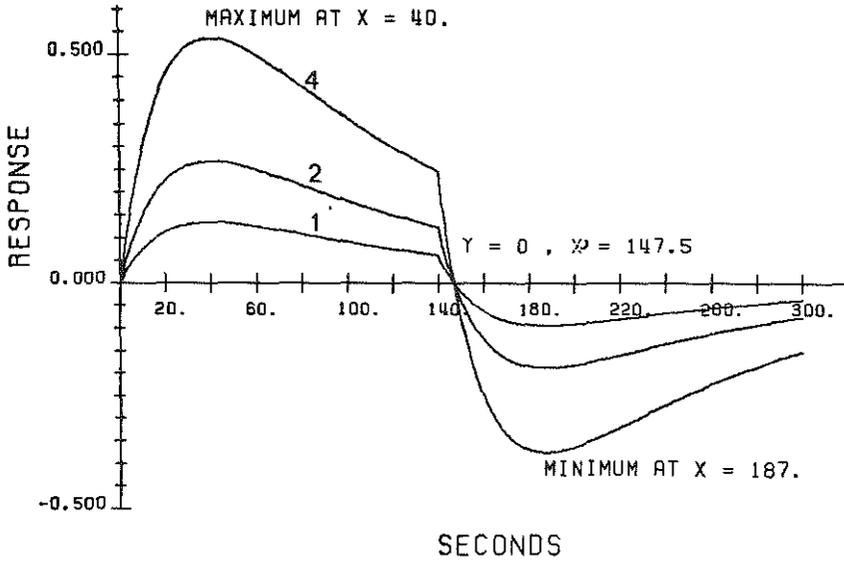
Fig. 2. Response of the second order model with adaptation to a constant acceleration of various amplitudes, lasting 140 s. Amplitude factor: 1, 2 and 4. Cupular T_1=20 s; T_2=0.01 s and T_a=100 s.
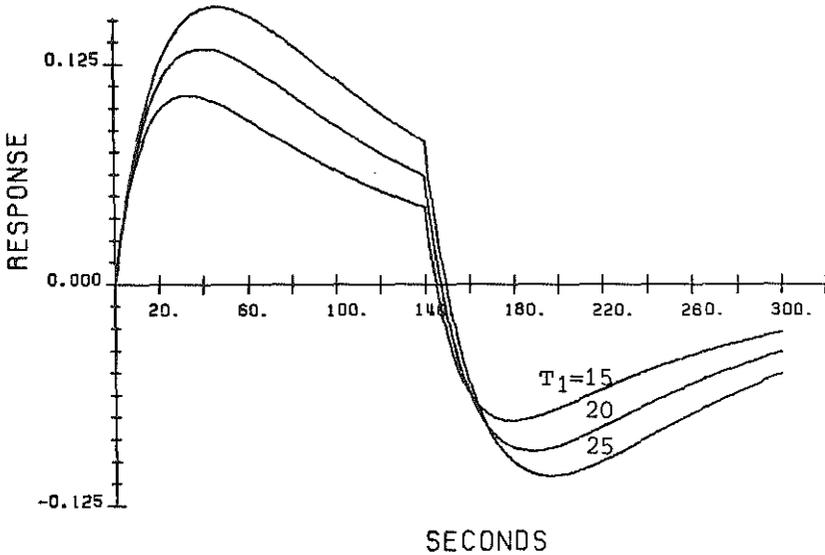
Fig. 3. Response, for various values of T_1, of the second order model with adaptation to a constant acceleration lasting 140 s. Amplitude factor: 1. Cupular T_1=15-20-25 s; T_2=0.01 s and T_a=100 s.
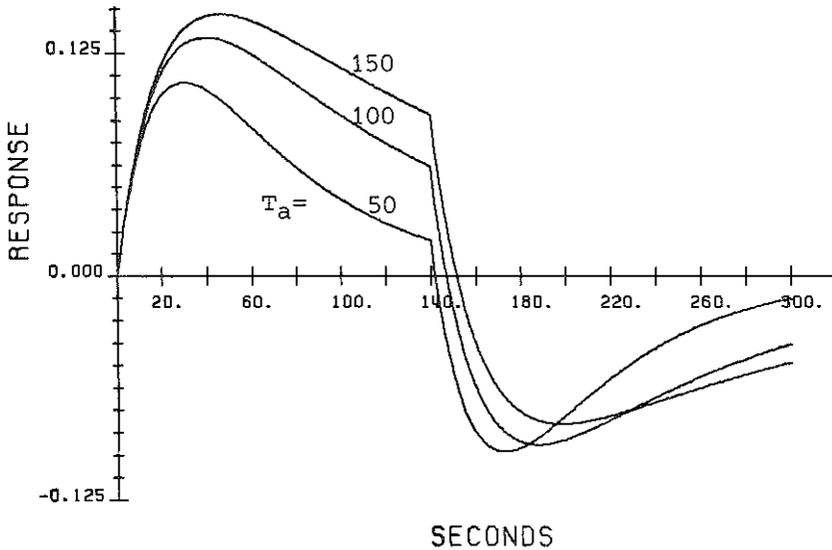
Fig. 4. Response, for various values of T_a, of the second order model with adaptation to a constant acceleration lasting 140 s. Amplitude factor: 1. Cupular T_1=20 s; T_2=0.01 s and T_a=50-100-150 s.
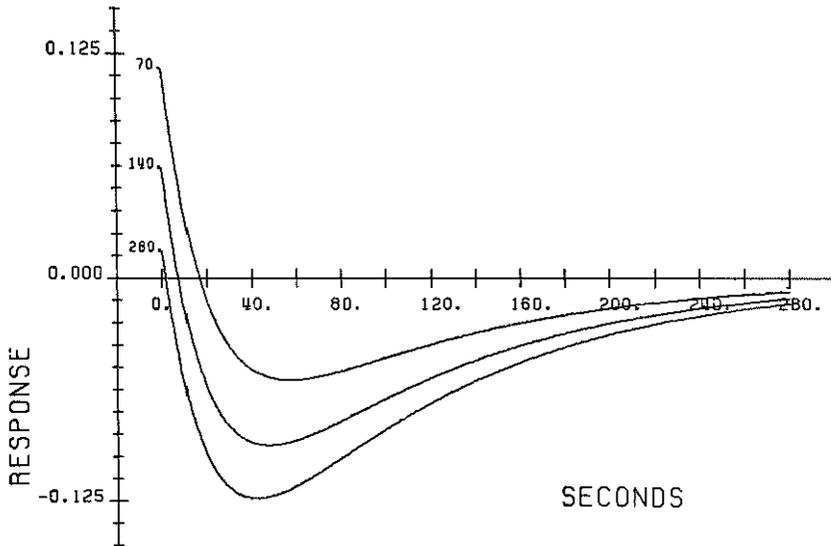

Fig. 5. Response, after various stimulus durations, of the second order model with adaptation after a period of constant acceleration. Preceding stimulus duration: 70-140-280 s. Amplitude factor: 1. Cupular T_1=20 s; T_2=0.01 s and T_a=100 s.

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In fig. 3 equations (4) and (5) have been plotted for values of the cupular time constant T_1 ranging from 15 to 25 seconds. The amplitude factor is unity. A higher value of T_1 results in an increase in the values of $Amax1$, Aa and $Amax2$, and increases the times of $t\ Amax1$, t_0 and $t\ Amax2$.

In fig. 4 the adaptation time constant T_a has been varied. The influence on the parameters is qualitatively the same as described for T_1, except for $Amax2$, which takes a lower value when T_a is increased. It can be seen that for the values of T_1 and T_a given in fig. 3 and fig. 4, a change in the value of T_a has a greater effect on the value of Aa, and thus on t_0, than a change in the value of T_1.

In fig. 5 it is the duration of the preceding acceleration period which is varied, from 70 to 280 s. The postacceleratory response curves are plotted. The longer the preceding acceleration period, the shorter is the time (t_0) required for the response to reverse direction, the larger is the secondary response ($Amax2$) and the earlier in the recovery period that the maximum of the reversed response ($t\ Amax2$) occurs.

Table I. Calculated values of various parameters of the response of the second order model with an adaptation term to a constant input. The values of T_1, T_a and stimulus duration are varied.

Time constants (s) inserted in eq.(4) and (5)	Stimulus duration	Amax1	t Amax1 (s)	Aa	% of Amax1	t_0 (s)	Amax2 (absol.)	% of Amax1	t Amax2 (s)
$T_2=0.01$ } $T_1=$ 15 $T_a=100$ 20 25	140 s 140 140	.107 .134 .157	35 40 46	.044 .061 .081	(41) (46) (52)	5.5 7.5 9.5	.077 .094 .108	(72) (70) (69)	38 47 56
$T_1=20$ } 50 $T_2=0.01$ $T_a=100$ 150	140 140 140	.109 .134 .147	31 40 47	.020 .061 .091	(18) (46) (62)	2.5 7.5 11.5	.098 .094 .083	(90) (70) (56)	33 47 58
$T_1=20$ } $T_a=100$ { $T_2=0.01$	70 140 280	}. 134	40	.117 .061 .015	(87) (46) (11)	16.5 7.5 1.5	.057 .094 .124	(43) (70) (93)	57 47 42

In table I the calculated values of the various parameters are summarized. The values of t_0 and $t\ Amax2$ are given with respect to Δt. The value (Aa) of the response at the end of the stimulus period (Δt) is determined by the values of T_1 and T_a. The value of Aa is also influenced by the stimulus amplitude factor and by the stimulus duration. In the table Aa is calculated for various values of T_1, T_a and stimulus duration holding the stimulus amplitude factor equal to unity.

Furthermore the value of Aa is given as a percentage of the corresponding value of $Amax1$. The decline from $Amax1$ to Aa is more pronounced when the value of either T_1 or T_a is low, and when the stimulus duration is long.

As can be seen in fig. 1 the maximum response of the VOR-system is lower than the final amplitude of the cupular displacement. When the stimulus amplitude is unity this cupular displacement is equal to the product of the time constants T_1 and T_2. In table II the maximum response ($Amax1$) is presented as a percentage of the final amplitude

Table II. *Comparison of the maximum response of the second order model, with and without an adaptation mechanism, to a constant input. The values of T_1 and T_a are varied.*

Second order model equation (1)	cupular displacement	sec.order model + adapt.mechan. equation (4)	Amax 1	% of cupular displacement
T_2=0.01 s } T_1=20s 15s 25s	0.150 0.200 0.250	T_2=0.01 s T_a=100 s } T_1=20 s 15 s 25 s	0.107 0.134 0.157	71 67 63
T_2=0.01 s T_1=20s	0.200	T_a=100 s 50 s 150 s	0.109 0.134 0.147	55 67 74

of the cupular displacement. The effect of adaptation appears to be greater when the cupular time constant T_1 has a high value or when the value of the adaptation time constant is low.

Table III. *Value of the adaptation time constant $T_a(s)$, estimated from the response decline of the second order model with adaptation, plotted on log-linear graph paper (decay method).*

Inserted in eq.(4)	Stimulus duration (s)			
	70	105	140	280
T_2=0.01 s T_a=100 s } T_1=20 s 15 s 25 s	T_a=128 190 ?	115 128 156	102 107 119	101 99 100
T_1=20 s T_2=0.01 s } T_a=100 s 50 s 150 s	80 190 ?	61 128 196	52 107 158	50 99 148

When the cupular deflection has achieved its final constant displacement, the response of the VOR-system will be influenced by the adaptation mechanism alone. By plotting the VOR-response on log-linear graph paper the adaptation time constant can be estimated from the decline of the peracceleratory response from Amax1 to Aa. An example is shown in fig. 6. In table III the estimated value of T_a is given for various values of T_1, T_a and stimulus duration. When the stimulus duration is too short, the estimated value of T_a tends to be much too high, especially when the value of T_1 is high.

Finally the time constants of the peracceleratory response rise (T_r) and of the postacceleratory response fall (T_f) are calculated. As indicated in fig. 1 the value of T_r is calculated by determining the point at which the peracceleratory response has risen to 63% of the value of Amax1. In order to calculate T_f the value of Aa and the absolute value of Amax2 are added together and the point is determined at which the response during the postacceleratory period has fallen by 63% of the sum. In table IV the values of T_r and T_f are given for various values of T_1, T_a and stimulus duration. The value of T_r expressed as a percentage of T_1 is lower, either when the cupular time constant T_1 is long or when T_a is short. The same is also true of T_f. With a stimu-

lus duration of 140 s the value of T_r is less than that of T_f. Table IV also shows that the longer the preceding acceleration period, the lower is the value of Tf.

Table IV. Calculated value of the time constant of the response rise (Tr) and fall (Tf) of the second order model with adapatation.

| Inserted in equation (4) and (5)		Stimulus Duration	T_r	% of cup.T₁	T_f	% of cup.T₁
T2=0.01 s Ta=100 s } T1=20 s	15 s	140 s	9.6	64	10.5	70
	20 s	140 s	11.8	59	13.2	66
	25 s	140 s	13.9	56	15.8	63
T1=20 s T2=0.01 s } Ta=100 s	150 s	140 s	9.4	47	9.9	50
	100 s	140 s	11.8	59	13.2	66
	150 s	140 s	13.2	66	15.1	76
T1=20 s T2=0.01 s } Ta=100 s	70 s				14.7	74
	140 s	}11.8	59		13.2	66
	280 s				12.2	61
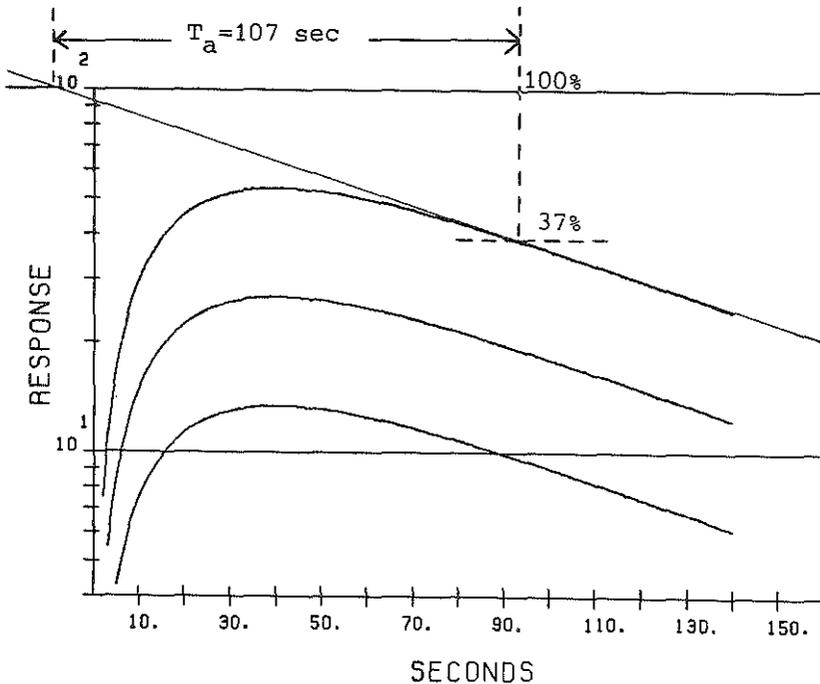
Fig. 6. Same as fig. 2, plotted on log-linear graph paper. The value of the adaptation time constant Ta, estimated by the decay method, is 107 s.

DISCUSSION

The maximum permissible stimulus velocity limits the duration and amplitude of constant acceleration in the experimental procedure. As can be deduced from the theoretical calculations, the *stimulus duration* should be as long as possible, about 140 s, since the value (Aa) of the response at the end of the stimulus period is then sufficiently low to be distinguished from the maximum peracceleratory response (Amax1). A long stimulus duration also means that the adaptation time constant T_a can be reliably calculated, while the secondary response becomes large enough to be distinguished from the zero response level.

The *stimulus amplitude*, on the other hand, should be as high as possible with respect to both the stimulus duration and the maximal permissible stimulus velocity. In fig. 2 the peracceleratory response decline appears to be more pronounced when the stimulus amplitude is large, whereas in fact the relative decline is the same for all three curves. However, it is easier to calculate the value of T_a from the upper curve. A remark must be made about the dependence of the maximum peracceleratory response on the value of the cupular T_1: because of the gain factors of the exponential powers, Amax1 becomes larger when a higher value of T_1 is inserted in equation (4). The magnitude of the secondary response behaves in a similar way.

In the postacceleratory period of constant velocity a higher value of T_a causes a reduction in the absolute value of Amax2 and prolonges the duration t Amax2. However the value of Amax2, and especially that of t Amax2, are usually difficult to estimate under experimental conditions and so cannot be regarded as reliable parameters.

The same interaction of T_1 and T_a is found in the calculation of the values of T_r and T_f as can be found in the calculation of the response T_1 from an impulse response when using the cupulometric and decay methods *(Boumans et al.,* 198.a and b, chapter II and III). Thus these parameters cannot be used reliably to calculate the cupular T_1 or the adaptation time constant T_a from the VOR-response to constant acceleration. The adaptation time constant T_a is calculated by plotting the peracceleratory response decline on log-linear graph paper. This method is only reliable when the stimulus duration is 140 s or more. In the next chapter *(Boumans et al.,* 198.f, chapter VII) we examine the literature to see which parameters have been used in the evaluation of the VOR-response during and after a period of constant angular acceleration. Furthermore the results of a pilot investigation in a small group of healthy subjects are reported.

CONCLUSION

With the addition of an adaptation term to the second order model of cupular behaviour the response of the VOR-system to a sufficiently long period of constant angular acceleration reaches a maximum followed by a decline, whereas in the post-acceleratory period a reversal in response occurs.

The time course of the response can be described by the values of the parameters Amax1, Aa, Amax2, t Amax1, t_o and t Amax2. These parameters are partially determined by the values of both the cupular T_1 and the adaptation time constant T_a.

When a constant angular acceleration with a duration of 140 s or more is used, the value of T_a can be estimated from the peracceleratory response decline and appears to be almost independent of the value of the cupular $T1$. Such independent estimation of Ta is not possible with impulsive or sinusoidal stimulation.

Unless the duration of the stimulus is very long the reversed response has a low value and t Amax2 is difficult to estimate.

For this reason the parameters Amax2 and t Amax2 are of little help in evaluating the VOR-response. The determination of the time t_0 at which the response reversal occurs seems to have more practical value. The values of the time constant of the response rise (T_r) and of the fall (T_f) are largely determined by the interaction of the cupular T_1 and the adaptation time constant T_a, as was also the case for the impulsive stimulation of the system. Conversely the values of $T1$ and of Ta cannot reliably be determined from these parameters.

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CHAPTER VII: RESPONSE OF THE HUMAN VESTIBULO-OCULAR REFLEX (VOR)
SYSTEM TO CONSTANT ANGULAR ACCELERATION

II.EXPERIMENTAL INVESTIGATION

ABSTRACT. The VOR-response to a constant angular acceleration
was investigated in a small group of subjects by varying the stimulus
amplitude and the stimulus duration. Various parameters of the response
were determined and compared with the results of the theoretical study
(Boumans et al., 198.e, chapter VI). This form of stimulation yields
a rather high value for the adaptation time constant T_a, which perhaps
indicates that there is an adaptation gain of less than unity. This
supposition is supported by finding of non-linearity within the VOR-
system at high stimulus amplitudes.

INTRODUCTION

It is well known that the vestibular response to a prolonged con-
stant angular acceleration may gradually decline after reaching a maximum
value, due to an adaptation mechanism.
This adaptation phenomenon has been demonstrated for the vestibular
sensation, by, among others, *Ek et al.*(1960) and *Guedry*(1974). In animal
experiments adaptation has been demonstrated within Scarpa's ganglion
in primates *(Goldberg and Fernandez,* 1971), in the posterior ampullary
nerve of the frog *(Taglietti et al.,* 1977) and in the second order neu-
rons of the cat *(Babin et al.,* 1980).
In the case of the human vestibulo-ocular reflex (VOR) the experi-
mental results obtained during and after constant angular acceleration
of a subject around the vertical axis differ from each other, as can be
seen from a survey of VOR data found in the literature.
Aschan and Bergstedt (1955) found that the occurrence of secondary
nystagmus was dependent on the duration of the primary nystagmus that
had been induced.
Ek et al.(1960) merely describe the VOR-response to a constant
acceleration and do not give experimental data.
Guedry and Lauver (1961) investigated, in 6 healthy subjects, the
peracceleratory nystagmus during constant accelerations of 2 and 1.5 °/s2
lasting for 45 and 60 s respectively. The maximum peracceleratory res-
ponse (Amax1) occurred at about 30 s. With the acceleration stimulus
of 2 °/s2, Amax1 amounted to 14-15 °/s slow phase eye velocity (SPV);
for 1.5 °/s2 it was 11.5-12.5 °/s SPV. After that little or no decline
in response was observed. After-nystagmus was not mentioned.
Collins and Guedry (1962) repeated the previous experiments while
keeping the subjects alert by arithmetical tasks. During mentally active
states no decline of nystagmus was evident. The value of Amax1 was found
to be slightly higher: 8-10 °/s SPV for a stimulus of 1 °/s2, and 17.5-
22 °/s SPV for 1.8 °/s2.
Later a higher stimulus value of 4 °/s2 was used *(Collins and
Guedry; Guedry and Collins,* 1967). No peracceleratory decline was found
when the stimulus duration was varied between 1 and 36 s. After the
stimulus duration of 36 s nystagmus reversal was observed. They also

observed a steeper decay in the postacceleratory period when the preceding stimulus duration was long and they mentioned this as circumstantial evidence for a "secondary process".

Brown and Wolfe (1969) investigated the VOR in 15 alert subjects. As a stimulus they used constant accelerations of 3-24 o/s^2 lasting for 88-10 seconds. With stimulus durations of 88 and 53 s Amax1 occured at 35 s and was followed by a decline in the peracceleratory response. In a further investigation in 10 subjects the moment at which Amax1 was reached (t Amax1) was found to be independent of the stimulus amplitude. The phenomenon of nystagmus reversal is only mentioned in passing.

Young and Oman (1969) and *Malcolm and Melvill Jones* (1970) have given the mathematical model of the adaptation mechanism. In the latter paper 8 subjects were tested, using a constant acceleration of 4.5 o/s2 lasting for 120 s. The result of one measurement is shown: Amax1 amounted to about 40 o/s SPV, whereas the secondary response maximum (Amax2) was about 20 o/s SPV. They compared the experimental responses with those derived from a theoretical model of the VOR-system, and determined quantitatively the time constants which describe the time course of the response to a constant angular acceleration. The mean time constant of the adaptation mechanism (T_a) was found to be 82 s (S.E. ± 6.5 s), and the mean cupular time constant T_1 was 21 s (S.E. ± 1.5 s).

McClure et al. (1973, 1976) determined the cumulative SP eye displacement during and after a constant angular acceleration of 3 o/s^2. Quantitative data cannot be derived from these papers.

Later they released two figures of the horizontal nystagmus response in normal subjects *(McClure et al.;* 1978): in one a distinct decline, in another no decline in peracceleratory response is shown.

Koenig et al. (1978) used acceleration stimuli of 3-12 o/s^2. The stimulus duration as only 10 s. They calculated the time constant of the postacceleratory decline in response and found its mean value to be 15.2 s (SD=7.2 s).

Finally, *Bock et al.* (1979) investigated 5 subjects by using a 2.5 o/s2 acceleration for 160 s. The results of two measurements were published, where the mathematical model, derived by *Young and Oman,* was fitted to the experimental data. In the discussion a value of 70-130 s was suggested for the adaptation time constant T_a.

Conclusion: Although a prolonged constant acceleration should in theory be a superior form of stimulation for investigating of the adaptation mechanism in the VOR-system, the results from the experimental data in the literature are incomplete and far from unanimous. From these data it appears that:
- The maximum peracceleratory response value, if present, is reached at about 35 s after the onset of the acceleration. The maximum value of SPV (expressed in o/s) amounts to about 10 times the value of the acceleration used (expressed in o/s2).
- A peracceleratory decline in response is not always observed. According to *Guedry* this decline does not occur in alert subjects.
- Only *Malcolm and Melvill Jones* have published data on the secondary response. This phenomenon is often not even mentioned in the literature.
- *Malcolm and Melvill Jones* found a fairly constant value for T_a in contrast with the findings of *Bock et al.*. Other investigators

do not give any value for the adaptation time constant.

Because of the limited data in the literature, we expected to encounter some experimental difficulties and therefore started a modest pilot investigation of the VOR-response to constant acceleration using only a few subjects. The purpose of this study was to discover reliable parameters to be used in the evaluation of the per- and postacceleratory VOR-response. Special attention was paid to the peracceleratory response decline, and to the moment of nystagmus reversal in the postacceleratory period. The experimental data so obtained are reported here and interpreted by means of the previous theoretical study *(Boumans et al., 198.e, chapter VI).*

METHOD

a. *Stimulus and experimental procedure*
The stimulus was a period of constant acceleration, in either a clockwise (CW) or a counter clockwise (CCW) direction. The stimulus was induced by a rotation room *(Teerhuis et al., 1979)* that rotated about a vertical axis. The subject was seated in a chair in such a way that his vertex was at the centre of rotation. All tests were done in complete darkness but the subject had his eyes open. He was kept alert by carrying out exercises in mental arithmetic during the trials.
The stimulus was centred on a condition of zero velocity and maximum room velocity was 150 ^{o}/s. The postacceleratory period of constant velocity lasted 5 minutes.
In one series of measurements, the stimulus amplitude was held constant at 2.15 ^{o}/s^2, with a duration varying from 70-140 s. The responses of 2 subjects were measured several times and an additional 4 subjects were investigated for a stimulus duration of 140 s.
In a second series of measurements, the amplitude was varied from 1-2.15-4.3 ^{o}/s^2 and the stimulus duration ranged from 290-70 s. In this series measurements were made on 3 subjects.

b. *Recording and data processing*
The horizontal nystagmus response was recorded using standard DC-electronystagmographic techniques. A technical description has been given elsewhere *(Boumans et al., 198.d, chapter V).* Data processing of all recordings was done by hand. Slow phase eye velocity (SPV) was plotted, and the peracceleratory response maximum (Amax1) and the time at which Amax1 was reached (t Amax1) were determined. The value (Aa) of the response at the end of the acceleration period, the time at which the postacceleratory response reversed direction (t_o) and the secondary response maximum (Amax2) during the period of constant velocity were all recorded. Finally the time constants of both the peracceleratory response rise (T_r) and the postacceleratory response fall (T_f) were calculated.

RESULTS

In the first series a stimulus amplitude of 2.15 ^{o}/s^2 was used. The results from the two subjects investigated are summarized in table I. The data for CW and CCW rotation have been amalgamated, because they

showed no systematic difference.

Table I. Mean values of various parameters of the VOR-response in two subjects. Stimulus: constant angular acceleration of 2.15 o/s². Amax1, Aa and Amax2 in o/s SPV. Time in seconds.

Subject	Stimulus duration	Amax1	t Amax1	Aa	t_o	Amax2	T_r	T_f	N
HS	70 s	16.3	34.5	10.9	17.0	4.9	13.5	16.3	12
	105 s	14.3	38.1	8.6	11.6	6.9	12.1	13.5	8
	140 s	15.4	34.1	7.1	9.7	7.6	13.9	13.1	12
	Mean	15.3	35.3						32
	S.D.	2.2	8.5						
RM	70 s	14.5	38.5	8.5	19.5	1.5	12.0	9.0	2
	105 s	14.0	37.0	8.5	14.5	2.5	14.0	11.5	2
	140 s	14.6	39.0	10.1	16.4	3.6	16.2	13.7	6
	Mean	14.4	38.7						10
	S.D.	2.5	3.1						

In <u>subject HS</u> Amax1 has a mean value of 15.3 o/s SPV which is reached after 35.3 s. When the stimulus duration is prolonged the mean peracceleratory response declines to 10.9 o/s at 70 s and to 7.1 o/s at 140 s. By plotting the mean Aa-values on log-linear paper the time constant of the peracceleratory decay (adaptation T_a) is estimated to be 151 s for this subject.
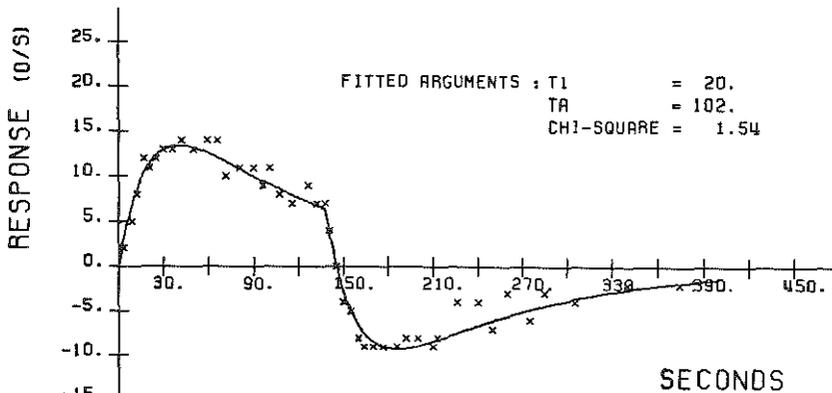

Fig. 1. Experimental data from a single test in subject HS, plotted, and fitted with the theoretically derived curve by the least squares method. Stimulus amplitude: 2.15 o/s2; stimulus duration 138 s.

In fig. 1 the experimental data for a single test with the stimulus duration of 138 s are fitted, by the least squares method, to equations (4) and (5) of the second order model with adaptation, as outlined in chapter VI *(Bouwans et al., 198.e)*. This example shows that the cupular

T_1 is 20 s, and T_a is 102 s.

In fig.2.a the mean values of Amax1, t Amax1, t_0 and Amax2 for the stimulus duration of 140 s, and the mean values of Aa at 70-105-140 s (see table I), are fitted to the theoretical curve, which was derived by means of the least squares method. The value of the cupular T_1 is found to be 18 s and that of T_a to be 132 s.

a. Subject HS

b. Subject RM
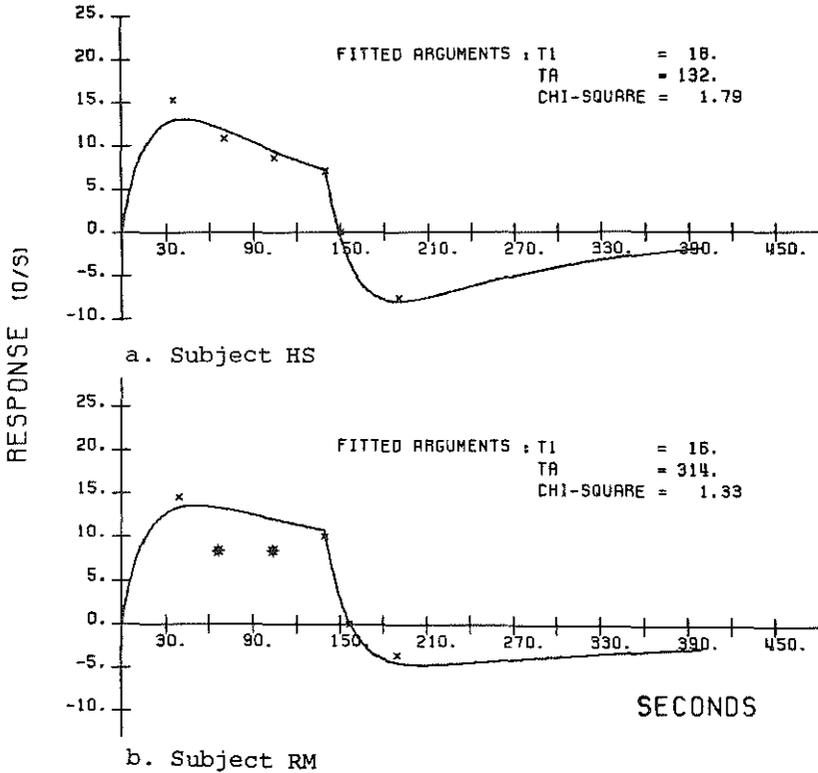
Fig. 2.a   *Subject HS. The mean response values, obtained from the VOR-responses during and after a constant angular acceleration of 2.15 o/s2, plotted, and fitted with the equations(4) and(5) of the second order model with adaptation (see Boumans et al., 198.e) by the least squares method.*

    b   *Subject RM. Same procedure as in fig. 2.a. The mean values of Aa at 70 s and 105 s (⁕) are not used in the fitting program.*

A reversal in response is observed in all measurings. The moment at which the response changes its direction is dependent on the duration of the preceding stimulus. The value of Amax2 is of the same order of magnitude as the value of the peracceleratory response decline. The moment of t Amax2 when the postacceleratory maximum occurred could not

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be reliably determined.

The time constant calculated from the peracceleratory response rise (T_r) and the postacceleratory response fall (T_f) are shown on the right hand side of table I. The method is the same as described in the previous chapter *(Bouwans et al., 198.e, chapter VI)*.

The number of measurements on subject RM is fewer than on the previous subject HS (table I). The mean value of Amax1 is found to be 14.4 °/s SPV at 38.7 s. The mean value (Aa) of the peracceleratory response at the end of a stimulus period of 140 s is higher than after a stimulus period of 70 s or 105 s. A similar phenomenon was observed in a peracceleratory response to a single stimulus lasting 140 s. For this reason the value of T_a could not be calculated from the decline of the mean response data in this subject.

In fig. 2.b the theoretical curve is fitted to the mean values of Amax1, t Amax1, Aa, t_0 and Amax2, measured with a stimulus of duration of 140 s. The mean values of Aa at 70 s and 105 s are inserted with an asterisk in the figure, but are not used in the curve fitting procedure. The cupular T_1 in this subject is found to be 16 s, while T_a is 314 s.

The values of Amax2 are low in comparison with the peracceleratory decline in response. The values of T_f are found to be less than those of T_r (Table I).

In another 4 subjects the peracceleratory parameters have been calculated from a series of tests with a stimulus of constant amplitude 2.15 °/s² and of duration 140 s, for both CW and CCW rotation.

Combining the mean values of the subjects HS and RM with these results the mean value of Amax1 for all 6 subjects is found to be 19.8 (SD=7.3) °/s SPV at 34.6 s (SD=8.4 s). The mean value of Aa is 9.2 (SD=6.6) °/s SPV for all 6 subjects together.

In the second series of measurements stimulus amplitudes were 1, 2.15 and 4.3 °/s². The results for three subjects are presented in table II and fig. 3.

Table II. Mean values of various parameters of the VOR-response in three subjects. Variable stimulus amplitude. Amax1 in °/s SPV; t Amax1 in seconds.

Subject	acc.(°/s²)	Stimulus duration	Amax1	S.D.	t Amax1	N
HS	1.0	290 s	7.2	2.4	--	2
	2.15	140 s	15.4	2.2	35	12
	4.3	70 s	36.6	5.3	33	5
RM	1.0	290 s	7.3	1.8	--	6
	2.15	140 s	14.6	2.5	39	6
	4.3	70 s	31.8	5.3	32	6
MR	1.0	290 s	18.4	3.8	--	9
	2.15	140 s	32.4	4.4	39	8
	4.3	70 s	57.0	7.1	34	4
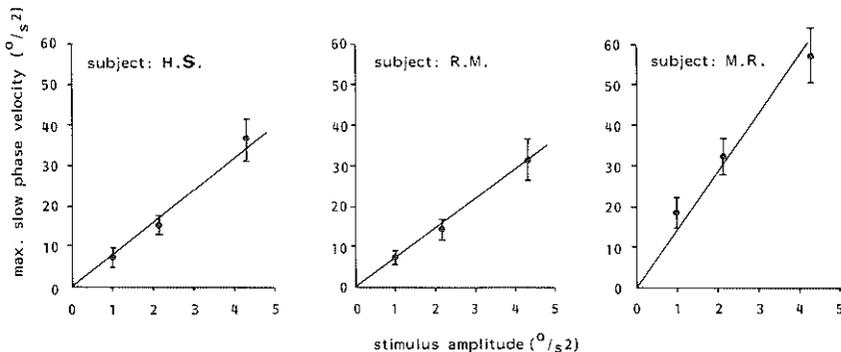
Fig. 3. Mean values of the peracceleratory VOR-response maximum (o/s SPV) for 3 stimulus amplitudes (o/s2), in 3 subjects (see table II). Bar represents 2xSD.

Since the value of t $Amax1$ seemed to be smaller where a higher stimulus amplitude was used an additional experiment was carried out on the subjects RM and MR, using an acceleration of 9.4 o/s^2 lasting for 32 s. The time t $Amax1$ was found to be 25 s and 20 s for RM and MR respectively; the values of $Amax1$ were found to be 68 and 89 o/s SPV. In another subject (LB) the value of t $Amax1$ changed from 40-26-14 s with the stimulus amplitudes of 2.15, 4.7 and 9.4 o/s^2 respectively; the values of $Amax1$ were 7, 25 and 35 o/s SPV.

For a long stimulus of duration 290 s and amplitude 1 o/s^2, the peracceleratory response declined to the zero velocity level in many of the measurements. Subsequently during the same period of acceleration the response sometimes reappeared. A peracceleratory response reversal was never observed.

DISCUSSION

In the subject HS the response of the VOR-system to a constant angular acceleration appears to be consistent with the theoretical response, calculated in the previous chapter VI*(Boumans et al., 198.e)*. After reaching a maximum value at about 35 seconds the peracceleratory response declines. When the stimulus ceases after a duration of 140 s the value of Aa amounts to 46% of $Amax1$.

According to the theoretical calculations *(Boumans et al., 198.e, chapter VI, table I)*, the value of the adaptation time constant T_a could lie between 100 s and 150 s, assuming a cupular T_1 of 15-20 s.

The value of T_a, calculated from the mean values of Aa that are registered at the end of the stimuli of various durations, is found to be 151 s. The fit for a single measurement (fig. 1) gives a value for T_a of 102 s.

Assuming a value for T_1 of 20 s and for T_a of 100-150 s, and a stimulus duration of 140 s, the time of the response reversal (t_o), calculated in the theoretical model with adaptation, is 7.5-11.5 s. The mean value of t_o in subject HS is 9.7 s for a stimulus of this duration.

The mean value of Amax2 (7.6 °/s SPV) amounts to 49% of Amax1 (15.4 °/s SPV). In the theoretical model (T_1=20 s, T_a=100-150 s) the value of Amax2 is 70-56% of the value of Amax1.

Summary: From the mean values of the various parameters of the per- and postacceleratory VOR-response in subject HS the value of the cupular T_1 is calculated to be 18 s, and that of T_a to be 132 s (fig. 2.a). The experimental value of t_0 lies very close to that given by the theoretical curve. The absolute value of Amax2 is low not only in comparison with the value suggested by the theoretical calculations but also with the values found experimentally for Amax1 and Aa.

In the subject RM there is a notable difference from the theoretical decline of the response: after reaching the maximum value the peracceleratory response declines to a level where it seems to remain constant, suggesting that the gain of the adaptation mechanism is less than unity. For this subject the value of T_a determined from the response to sinusoidal oscillation was remarkably high, being 230 s *(Boumans et al., 198.d, chapter V)*. This high value of T_a explains to some extent the high value of Aa after a stimulus of duration 140 s (fig. 2.b). In an additional experiment with a constant acceleration of 1 °/s^2 lasting for 290 s the subject RM showed a response decline from 7 °/s (Amax1) to 2 °/s (Aa) suggesting that the adaptation gain is, after all, equal to unity. However, for these long test stimulations a lack of alertness may be an important reason for the decline in response.

In this subject t_0 is rather long, but this is consistent with the high value determined for T_a. The mean value of Amax2 amounts only to 25% of the mean value of Amax1. The last two results appear to be in contradiction with the relatively low value found for T_f (see table I). This shows that the time constant of the postacceleratory decline in response is not a reliable parameter on which to base an evaluation of the VOR-response. On the contrary, a low value of T_f suggests a steep postacceleratory decline, whereas, in fact, the postacceleratory response course is characterised by a relative slow and flat decay in this subject RM as in other subjects.

The low value of T_f appears to be related to an initial fast postacceleratory decline, after which the curve becomes flat in the region of the zero response level.

Summary: In subject RM the initial rapid decline in peracceleratory response cannot be accounted for by the theoretical model used in the previous chapter *(Boumans et al., 198.e, chapter VI)*: it is thus impossible to calculate T_a from the mean values of Aa for stimuli of various durations. The value of Amax2 in this subject is lower than would be expected from the theory.

It is interesting to note that the value of t Amax1 becomes less when higher stimulus amplitudes are used. In a pure linear system this time should be constant. Up to a stimulus amplitude of 4.3 °/s^2 the system was very close to linear (fig. 3), although the value of t Amax1 was already becoming slightly less. With a stimulus amplitude of 9.4 °/s^2 there was a distinct decrease in the value of t Amax1 for all 3 subjects.

For the explanation of this reduction in t Amax1 the following possibilities were considered:

(1)Saturation of SPV does not seem to play any part in reducing t Amax1, as is shown by the corresponding values of Amax1.

(2)The reduction in t Amax1 could also be caused by the cupula becoming locked at a certain degree of angular deflection. In table II of the previous chapter *(Boumans et al.,* 198.e, chapter VI) the theoretical relation between the cupular displacement and the maximum VOR-response has been calculated for various values of T_1 and T_a. In the case of a constant input the maximum value of the VOR-response is indeed rather low in comparison with the corresponding cupular displacement, due to the influence of the adaptation term. However, locked cupular displacement does not seem a very plausible assumption due to the fact that Amax1 increases steadily with stimulus amplitude, up to 9.4 $°/s^2$.

(3)Finally the gain of the adaptation mechanism should also be taken into account. In theoretical studies this factor is usually taken as unity. However, *Goldberg and Fernandez* (1971) found that while many neurons showed clear evidence of adaptation, there where other neurons which did not adapt. As noted by *Bock et al.*(1979):*"Taglietti et al.* (1977) showed that greater vestibular stimuli lead to recruitment of more adapting fibres, so adaptation can be expected to be more prominent if greater stimuli are used. The dependence of adaptation on stimulus strength should therefore be investigated more thoroughly". Thus, the gain of the adaptation mechanism could be expected to be less than unity when slow stimulus amplitudes are used. Conversely, during a very prolonged constant angular the peracceleratory VOR-response tends to decline to the zero response level, as is evidenced even in subject RM. This suggests an adaptation gain equal to unity.

Summary: The VOR-system shows non-linearity when the response to a constant angular acceleration is tested with a stimulus of high amplitude. The gain of the adaptation mechanism appears to vary with the stimulus amplitude. The fact that the gain is low when the stimulus amplitude is small accounts for the relatively high values of T_a found in our experiments. This phenomenon could be of clinical importance, in cases where a damaged peripheral vestibular sense organ results in a constant input into the central part of the vestibular system.

CONCLUSION

Consistent with the theoretical prediction the response of the human VOR-system to a long period of constant angular acceleration shows a peracceleratory decline in response, while in the postacceleratory period of constant velocity the response reverses direction.

However, although only a few subjects have been investigated, the results suggest that there are some significant discrepancies between theory and experiment:

- In this experimental situation the effect of adaptation is less than one would expect from the theoretical calculations: the value of the response at the end of the stimulus period is relatively higher than expected, whereas the postacceleratory decay is flat in the region of the zero response level. This results in a high value for the adaptation time constant T_a, when estimated from the experimental data. It is suggested that this can be explained by assuming that the adaptation gain is less than unity.

- At high stimulus amplitudes the VOR-system displays non-linearity. An adaptation gain dependent on the stimulus amplitude could account for this phenomenon.

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GENERAL DISCUSSION

From the results obtained during these investigations of the
human VOR-system it appears that the second order model with an adap-
tation term gives a close prediction of the VOR-response to the three
different types of stimulation. The adaptation mechanism explaines:
- the reversal in response after an impulsive stimulation,
- the phase lead of more than 90 degrees in sinusoidal stimulation
  at low frequencies, and
- the peracceleratory decline in response during constant angular
  acceleration of the VOR-system.

To ascertain exactly the extent to which the second order model
with adaptation can account for the VOR-response, the experimental
results obtained using the various stimuli in the small but fairly
constant group of subjects are compared and contrasted.

I. Comparison of the gain of the VOR-system
If it is assumed that the angular velocity of slow phase nystagmus
is proportional to cupular displacement, θ_c, then the second order model
of cupular behaviour should fully account for the response of the VOR-
system. The constant of proportionality, G_1, is equal to the ratio
between the slow phase eye velocity $\dot{\theta}_e$ (expressed in o/s) and the
corresponding cupular displacement θ_c (expressed in degrees):

$$\dot{\theta}_e = G_1 \cdot \theta_c \qquad\qquad (1)$$

The response of the second order model is altered by the introduction
of the adaptation mechanism. This modification can be described by a
varying term which is dependent upon the time constants of the system
and the type of stimulus used. This term, F_a expresses the ratio between
the responses of the second order model with and without adaptation.

$$\dot{\theta}_e = F_a \cdot G_1 \cdot \theta_c \qquad\qquad (2)$$

With this knowledge the value of G_1 can be calculated from the experi-
mental results obtained with the 3 stimuli.

1. Under *impulsive stimulation* the VOR gain, i.e. the ratio
between the maximum SPV (o/s) and the corresponding impulse amplitude
(o/s), was calculated for all subjects (N=6) and all measurements (N=287)
with stimulus amplitudes 25-50-100 o/s. The stimulus amplitude of
140 o/s was not included in this calculation, because saturation

N.B. The term G_1 has for simplicity been omitted throughout the
thesis, including the appendix.

occurred at this higher velocity. The VOR gain was found to be 0.66 (SD=0.10), i.e. the maximum value of the VOR-response is 0.66 $^{\circ}$/s SPV when a stimulus amplitude of unity (1 $^{\circ}$/s) is used.
The angular deflection of the cupula as a result of impulsive stimulation can be calculated by means of equation (3) in chapter II:

$$\theta_c(t) = o \qquad\qquad\qquad\qquad \text{for } t = <o$$

$$\theta_c(t) = \frac{T_1 \cdot T_2}{T_1 - T_2} \ (e^{-t/T_1} - e^{-t/T_2}) \qquad\qquad \text{for } t > o \qquad\qquad (3)$$

The maximum deflection of the cupula after an impulsive stimulus of unity is:

$$\theta_c = \frac{T_1 \cdot T_2}{T_1 - T_2} \approx T_2 \qquad\qquad\qquad\qquad\qquad\qquad (4)$$

(see chapter II, fig. 1)

When T_2=0.01 s, then θ_c=0.01 deg.
    The addition of the adaptation term does not influence the calculation of the maximum value of the VOR-response after an impulsive stimulation. This was demonstrated in chapter II (compare fig. 1 and fig. 4) and it is also demonstrated here. The response of the second order model with adaptation to an impulse is given by equation (6) in chapter II:

$$\dot{\theta}_e(t) = o \qquad\qquad\qquad\qquad\qquad\qquad \text{for } t = <o$$

$$\dot{\theta}_e(t) = \frac{T_1 \cdot T_2 \cdot T_a}{T_1 - T_2} \{ \frac{1}{T_a - T_1} \cdot e^{-t/T_1} - \frac{1}{T_a - T_2} \cdot e^{-t/T_2}$$

$$+ (\frac{1}{T_a - T_2} - \frac{1}{T_a - T_1}) \cdot e^{-t/T_a} \} \qquad \text{for } t > o \qquad\qquad (5)$$

where $\dot{\theta}_e$=angular eye velocity.
The maximum value of the response after an impulsive stimulus of unity is:

$$\dot{\theta}_e = \frac{T_1 \cdot T_2 \cdot T_a}{(T_1 - T_2)(T_a - T_2)} \approx T_2 \qquad\qquad\qquad\qquad (6)$$

(see chapter IV, fig. 4)

    Conclusion: When calculating the maximum value of the VOR-response to an impulsive stimulation the appropriate value of F_a appears to be 1. Thus the value of G_1 can be calculated by means of equation (2)=(1):

$$0.66 \ ^{\circ}/s = G_1 \times 0.01 \text{ deg} \qquad\qquad G_1 = 66/s \qquad\qquad (7)$$

    2. The same procedure can be followed in the case of *sinusoidal stimulation.*
    Under sinusoidal stimulation the VOR gain, i.e. the ratio between the peak SPV ($^{\circ}$/s) and the peak stimulus velocity ($^{\circ}$/s) at the same frequencies, was calculated for all subjects (N=7) and all measurements (N=25) for the frequency of 0.1 Hz (see chapter V, table I). The VOR

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gain at this frequency was found to be 0.68, i.e. at 0.1 Hz the peak
VOR-response is 0.68 °/s for a stimulus amplitude of unity (1 °/s).
According to the second order model the amplitude ratio, α, between
the peak deflection of the cupula and the stimulus amplitude (°/s) is
given by equation (2) in chapter IV:

$$\alpha = \frac{\omega \; T_1 \cdot T_2}{\sqrt{(\omega T_1)^2+1} \cdot \sqrt{(\omega T_2)^2+1}} \qquad (8)$$

where ω=freq. in radians/s; ω=2πxfreq.
Under sinusoidal stimulation with a stimulus amplitude of unity the
amplitude of the deflection of the cupula reaches its maximum at mid-
frequencies (0.05-5 Hz):

$$\theta_c = \frac{\omega \; T_1 \cdot T_2}{\omega \; T_1} = T_2 \qquad (9)$$

(see chapter IV, fig. 1)

When T_2=0.01 s, then θ_c=0.01 deg.

   Adding the adaptation term to the second order model results in
the following amplitude ratio, which is the same as equation (6) in
chapter IV:

$$\alpha = \frac{\omega^2 \; T_1 \cdot T_2 \cdot T_a}{\sqrt{(\omega T_1)^2+1} \cdot \sqrt{(\omega T_2)^2+1} \cdot \sqrt{(\omega T_a)^2+1}} \qquad (10)$$

The value of the response reaches its maximum at mid-frequencies:

$$\dot{\theta}_e = \frac{\omega^2 \; T_1 \cdot T_2 \cdot T_a}{\omega \; T_1 \cdot \omega \; T_a} = T_2 \qquad (11)$$

which is the same as in equation (9) for the pure second order system.
   Conclusion: When calculating the VOR-response to sinusoidal sti-
mulation at mid-frequencies the value of F_a appears to be 1. Thus, the
value of G_1 can be calculated by means of equation (2)=(1):

$$0.68 \text{ °/s} = G_1 \times 0.01 \text{ deg} \qquad G_1 = 68/_s \qquad (12)$$

   3. In order to calculate the value of G_1 for the VOR-system under
the stimulus of *constant acceleration* the maximum value of the per-
acceleratory response (Amax1) during constant acceleration of 2.15 °/s2.
was determined. The mean value of Amax1 was found to be 19.8 °/s for
6 subjects and 32 measurements (see chapter VII, results). Linearity
of the VOR-system was demonstrated in chapter VII (see fig. 3). Thus,
the maximum VOR-response to a constant stimulus of 1 °/s2 will be 9.2 °/s.
   The response of the second order model of cupular behaviour to
a step input is given in chapter VI, equation (1):

$$\theta_c(t) = o \qquad\qquad\qquad\qquad\qquad \text{for } t=<o$$
$$\theta_c(t) = T_1 \cdot T_2 (1- \frac{T_1}{T_1-T_2} \cdot e^{-t/T_1} + \frac{T_2}{T_1-T_2} \cdot e^{-t/T_2}) \text{ for } t > o \qquad (13)$$

According to this model the cupular deflection reaches a maximum after

a period of 4-5 times the cupular time constant T_1. For a stimulus amplitude of unity this maximum deflection of the cupula is:

$$\theta_c = T_1 . T_2 \tag{14}$$

When $T_1=20$ s and $T_2=0.01$ s, then $\theta_c=0.20$ deg.

The response of the second order model with an adaptation term to a step input is:

$$\hat{\theta}_e(t) = o \qquad\qquad\qquad\qquad \text{for } t = < o$$

$$\hat{\theta}_e(t) = \frac{T_1 . T_2 . T_a}{T_1 - T_2} \{ \frac{T_1}{T_a - T_1} (1 - e^{-t/T_1}) - \frac{T_2}{T_a - T_2} (1 - e^{-t/T_2})$$

$$\tag{15}$$

$$+ (\frac{T_a}{T_a - T_2} - \frac{T_a}{T_a - T_1}) (1 - e^{-t/T_a}) \} \qquad \text{for } t > o$$

(see chapter VI, eq.(4))

The peracceleratory response reaches a maximum (Amax1) at t Amax1 after which it declines, as can be seen in chapter VI, fig. 1. The maximum response of the second order model with adaptation is lower than the final amplitude of the cupular deflection. In table II of chapter VI the value of Amax1 is presented as a percentage of the final amplitude of the cupular displacement. This percentage is equal to the value of F_a, the ratio between the responses of the second order system with and without adaptation. For $T_1=20$ s, $T_2=0.01$ s and $T_a=100$ s:

$$F_a = 0.67 \tag{16}$$

Conclusion: When calculating the peracceleratory maximum of the VOR-response to a constant acceleration, the value of F_a appears to be 0.67, for $T_1=20$ s, $T_2=0.01$ s and $T_a=100$ s. The corresponding value of G_1 can be calculated by means of equation (2):

$$9.2 \; o/s = 0.67 \times G_1 \times 0.20 \text{ deg.} \qquad G_1 = 69/s \tag{17}$$

For $T_1=20$ s, $T_2=0.01$ s and $T_a=125$ s:

$$F_a = 0.70, \text{ thus } G_1 = 66/s \tag{18}$$

CONCLUSION

When the responses of the VOR-system to the 3 different stimuli are compared it can be seen that the values of G_1 shown in (7), (12) and (18) are in close agreement . It may be concluded that the second order model with adaptation accounts very well for the VOR-response.

*II. Comparison of the values for the cupular time constant T_1,
calculated from the VOR-responses to the 3 different stimuli*

1. From the *impulse response* of the VOR-system the value of the
long time constant T_1 was calculated for 5 subjects using two different
methods. In chapter I the decay method was used and the mean value of
the response T_1 was found to be 13 s.

Using the cupulometric method with a fixed threshold for SPV,
T_1 was 11.7 s (see chapter III).

A comparison of these experimental results with the results of
the theoretical study in chapter II suggests that in reality the cupu-
lar time constant T_1 is about 20 s, when T_a=100-125 s.

2. Under *sinusoidal stimulation*, the theoretical phase charac-
teristic of the VOR-response was fitted to the experimental data for
7 subjects, giving a cupular time constant T_1 of 16.6 s (see chapter V,
fig. 8).

3. In the investigation of the VOR-response to *constant angular
acceleration* the cupular T_1 was calculated in only three cases (see
chapter VII, fig. 1 and 2) and was 16-18-20 s.

CONCLUSION

The values of the cupular time constant T_1, determined from the
responses of the human VOR-system to 3 types of stimulation, are in
agreement and have a value of 20 s or slightly less.

*III. Comparison of the values for the adaptation time constant T_a,
calculated from the responses of the VOR-system to the 3 different
stimuli.*

1. A comparison between the experimental results and the theore-
tical calculations for the VOR-response to an impulsive stimulation
showed that the value of T_a was 100-125 s, for T_1=20 s (see chapter II
and III).

2. When the theoretical phase characteristic was fitted to the
experimental data, the value of T_a was found to be 114 s (see chapter
V, fig. 8).

3. In the experiments to determine the VOR-response to constant
acceleration, the value of T_a was 102-132-314 s (see chapter VII, fig. 1
and fig. 2).

CONCLUSION

The value of the adaptation time constant T_a, determined from the
responses of the human VOR-system to 3 types of stimulation, appears to
be about 100-125 s. However, it was found that the values of T_a varied
widely between subjects.

From this study of the VOR gain and of the time constants it can be concluded that the second order model with adaptation provides a very good account of the VOR-response to all three stimuli.

Finally it may be useful to comment on some of the specific results obtained in the various experiments.

A study to determine which type of stimulation is the most suitable for investigating adaptation within the VOR-system showed that the value of T_a could be reliably estimated from the theoretical peracceleratory decline in response during a period of constant acceleration. When the stimulus duration was long, this estimate of T_a proved to be almost independent of the value of the cupular T_1. Such an independent estimate of T_a was not possible using either impulsive or sinusoidal stimulation.

In the experimental situation, however, the estimation of T_a was difficult because the gain of the adaptation mechanism was also unknown. It should be repeated here that only a few measurements were done and that lack of alertness may also have a significant influence on the results obtained.

It is interesting to note that, for all the amplitudes used, the maximum of the VOR-response after an impulsive stimulation was always found to occur about 4-6 seconds after the beginning of the impulse (see chapter II, fig. 3). The duration of the impulse itself was never longer than 2.5 s (chapter III). The maximum response to an impulse is theoretically reached at about 0.07 s (chapter II). Further, the conduction time within the reflex arc is a few milliseconds. From the available literature it appears that the latency time of the human VOR-response to an impulsive stimulation has not been investigated. It is still not understood why there is such a long delay before the maximum of the VOR-response to an impulse is reached.

In the series of experiments using impulsive stimulation the stimuli were always given with increasing amplitudes, alternately in the CW and CCW directions. No order effects were encountered in the calculation of T_1, nor in the calculation of the value of the response maximum, nor in that of the time at which the response changed direction.

A similar situation occurred in the experiments with sinusoidal stimulation. No order effects were found within or between the test sequences. To minimize any possible effects of habituation one or more weeks were allowed to elapse between the test sequences. In the investigation of the frequency response of the VOR in the monkey, *Buettner et al.* (1981) found that animals which had previously been exposed to numerous rotatory stimuli showed much shorter time constants T_1 and T_a that did 'naive' animals. Although the subjects used in this investigation had some experience in vestibular experiments, it is unlikely that there was any modification of the subjects' VOR-response to sinusoidal stimulation due to habituation.

The functioning of the human VOR-system appeared to be linear under all 3 types of stimulation. However, when an impulsive stimulus was used, saturation of SPV occurred with stimulus amplitudes greater than 100 ^{o}/s. Non-linarity also appeared during constant acceleration at the high amplitude of 9.4 $^o/s^2$, the time at which the peracceleratory

response maximum was reached becoming shorter. However, this pilot investigation consisted of only a few experiments and further investigations should be done in this area.

Although the introduction of the adaptation mechanism has provided more insight into the functioning of the human VOR-system, the exact location of this mechanism remains unknown. In animal experiments a peripheral location has been demonstrated by *Taglietti et al.*(1977), who investigated the vestibular response in the posterior ampullary nerve of the frog. However, it should be assumed that there are several locations, which are probably central, since the value of the adaptation time constant T_a differs according to wether it is derived from the VOR-response or from the vestibular sensation. It is also at this central level that the time constant of the adaptation mechanism can be modified during normal daily life or by vestibular training.

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APPENDIX

MATHEMATICAL MODEL OF THE VESTIBULO-OCULAR REFLEX (VOR) SYSTEM

A. *Second order model*

The torsion-pendulum model of the semicircular canals was put forward by *Steinhausen* (1933). In this model the cupula-endolymph system is treated as a heavily damped, second order linear system, the angular displacement of the cupula (θ_c) being related to the input angular head acceleration ($\ddot{\theta}_h$) by the differential equation:

$$I\ \ddot{\theta}_h(t) = I\ \frac{d^2\theta_c}{dt^2} + B\ \frac{d\theta_c}{dt} + K\ \theta_c \tag{1}$$

where I=moment of inertia;
   B=viscous-damping couple;
   K=elastic-restoring couple.
In Laplace notation the transfer function of this system is:

$$H(s) = \frac{\theta_c(s)}{\theta_h(s)} = \frac{I}{Is^2+Bs+K} = \frac{I/K}{(I/K)s^2+(B/K)s+1} \tag{2}$$

Factorizing the denominator on the extreme right, eq.(2) can be written as:

$$H(s) = \frac{I/K}{(T_1s+1)(T_2s+1)} \tag{3}$$

where:

$$T_1.T_2=I/K, \text{ and } T_1+T_2=B/K \tag{4}$$

Van Egmond et al.(1949) showed experimentally that the value of T_1 is much higher than the product of the time constants T_1 and T_2; consequently $T_1>>T_2$, so that $T_1+T_2=B/K$ can be approximated by:

$$T_1=B/K \tag{5}$$

Using this approximation the first part of eq.(4) may be written as:

$$T_1.T_2=\frac{B}{K}\ .\ T_2=\frac{I}{K}, \text{ and hence: } T_2=I/B \tag{6}$$

Therefore B/K >> I/B, or B^2 >> IK.
Thus B is large relative to I and K and the sytem is heavily damped.
Let k=I/K. Then the transfer function of eq.(3) becomes:

$$H(s)=\frac{\theta_c(s)}{\theta_h(s)} = \frac{k}{(T_1s+1)(T_2s+1)} \tag{7}$$

The block diagram of this function is presented in fig. 1.
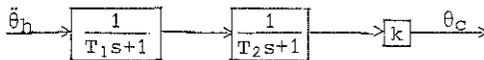
Fig. 1.

1. *Response of the second order system to an impulse*

The method of partial fractions can be used to calculate the step and impulse responses of the system. This method shows that two first order systems in cascade are equivalent to two first order systems connected in parallel. This can be demonstrated as follows. Suppose that it is possible to find two numbers A and B, such that:

$$\frac{1}{(T_1s+1)(T_2s+1)} \equiv \frac{A}{T_1s+1} + \frac{B}{T_2s+1}$$

Then $AT_2s+A+BT_1s+B \equiv 1$
Hence $AT_2+BT_1=0$ and $A+B=1$
Solution for A and B gives:

$$A = \frac{T_1}{T_1-T_2} \ , \text{ and } B = \frac{-T_2}{T_1-T_2} \ .$$

So eq.(7) is equivalent to:

$$H(s) = k\left(\frac{\frac{T_1}{T_1-T_2}}{T_1s+1} - \frac{\frac{T_2}{T_1-T_2}}{T_2s+1} \right) \tag{8}$$

or, as a block diagram:
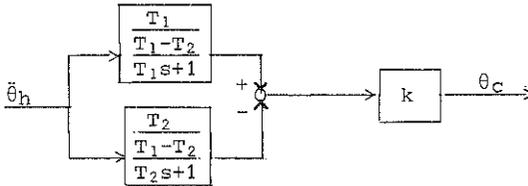
Fig. 2.

The unit impulse response of a first order system is:

$$y(t) = 0 \qquad\qquad \text{for } t \leq 0$$
$$y(t) = \frac{e^{-t/T}}{T} \qquad\quad \text{for } t > 0$$

The response of the transfer function (8) to a step change in angular velocity is, in the real time domain:

$$\theta_C(t) = 0 \qquad\qquad\qquad\qquad\qquad \text{for } t \leq 0$$
$$\theta_C(t) = k\left(\frac{1}{T_1-T_2}\cdot e^{-t/T_1} - \frac{1}{T_1-T_2}\cdot e^{-t/T_2}\right) \text{ for } t > 0$$

which can be written as:

$$\theta_C(t) = 0 \qquad\qquad\qquad\qquad \text{for } t \leq 0$$
$$\theta_C(t) = \frac{T_1\cdot T_2}{T_1-T_2}(e^{-t/T_1} - e^{-t/T_2}) \qquad \text{for } t > 0 \tag{9}$$

2. *Response of the second order system to a step input*

The response of a first order system to a unit step is:

$$y(t) = 0 \qquad\qquad \text{for } t \leq 0$$
$$y(t) = 1-e^{-t/T} \qquad \text{for } t > 0$$

The response of the transfer function (8) to a step acceleration is, in the real time domain:

$$\theta_c(t) = 0 \qquad\qquad\qquad\qquad\qquad\qquad \text{for } t \le 0$$

$$\theta_c(t) = k\left(\frac{T_1}{T_1-T_2} - \frac{T_1}{T_1-T_2}\cdot e^{-t/T_1} - \frac{T_2}{T_1-T_2} + \frac{T_2}{T_1-T_2}\cdot e^{-t/T_2}\right) \text{for } t > 0$$

which can be written as:

$$\theta_c(t) = 0 \qquad\qquad\qquad\qquad\qquad\qquad \text{for } t \le 0 \qquad\qquad (10)$$

$$\theta_c(t) = T_1\cdot T_2\left(1 - \frac{T_1}{T_1-T_2}\cdot e^{-t/T_1} + \frac{T_2}{T_1-T_2}\cdot e^{-t/T_2}\right) \text{for } t > 0$$

A constant acceleration equal to unity and of finite duration (Δt) is identical to a unit step at $t=0$ minus a unit step at $t=\Delta t$.
So the response of the function (8) to such a stimulus is, in the real time domain:

$$\theta_c(t) = 0 \qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad \text{for } t \le 0$$

$$\theta_c(t) = T_1\cdot T_2\left(1 - \frac{T_1}{T_1-T_2}\cdot e^{-t/T_1} + \frac{T_2}{T_1-T_2}\cdot e^{-t/T_2}\right) \qquad \text{for } 0 < t \le \Delta t$$

$$\theta_c(t) = T_1\cdot T_2\left\{\frac{T_1}{T_1-T_2}\left(e^{-(t-\Delta t)/T_1} - e^{-t/T_1}\right)\right. \qquad\qquad\qquad (11)$$

$$\left. + \frac{T_2}{T_1-T_2}\left(e^{-t/T_2} - e^{-(t-\Delta t)/T_2}\right)\right) \qquad \text{for } t > \Delta t$$

3. *Response of the second order system to a sinusoidal input*

When a linear system is subjected to a sinusoidal input the output, after a steady state of harmonic oscillation has been attained, is also sinusoidal and of the same frequency, although it generally has a different amplitude and phase. The output-input amplitude ratio and phase relationship are usually presented in so-called Bode plots.
The amplitude ratio (α) and phase relationship (ϕ) can be calculated from the transfer function if s is replaced by $j\omega$. In this way eq.(7) becomes:

$$H(j\omega) = \frac{k}{(j\omega T_1 + 1)(j\omega T_2 + 1)}$$

$$\alpha = \frac{\theta_c}{\overline{\theta_h}} = |H(j\omega)| = \left|\frac{k}{(j\omega T_1 + 1)(j\omega T_2 + 1)}\right|$$

$$\phi = \arg H(j\omega) = \tan^{-1}\frac{Im}{Re}$$

In the real time domain the amplitude ratio is:

$$\alpha = \frac{T_1\cdot T_2}{\sqrt{(\omega T_1)^2 + 1}\cdot\sqrt{(\omega T_2)^2 + 1}} \qquad\qquad\qquad (12)$$

The phase relationship is:

$$\phi = -\tan^{-1}(\omega T_1) - \tan^{-1}(\omega T_2) \qquad\qquad\qquad (13)$$

In the Bode plot the velocity output is usually compared with the velocity input. In equations (12) and (13) the displacement output is compared

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with the acceleration input. The transfer function $H(s)=\frac{\theta_c}{\theta_h}$ has to be transformed to $H(s)=\frac{\dot{\theta}_c}{\dot{\theta}_h}$, where $\theta_h=s\ \theta_h$. On the assumption that the slow phase eye velocity $(\dot{\theta}_e)$ is proportional to the cupular displacement (θ_c), $\dot{\theta}_c$ can be replaced by $\dot{\theta}_e$. Thus eq.(7) becomes:

$$H(s)=\frac{\dot{\theta}_e(s)}{\theta_h(s)} = \frac{ks}{(T_1 s+1)(T_2 s+1)} \tag{14}$$

In the real time domain the amplitude ratio is:

$$\alpha= \frac{\overline{\dot{\theta}}_e}{\overline{\dot{\theta}}_h} = \frac{\omega\ T_1 \cdot T_2}{\sqrt{(\omega T_1)^2+1}\ \cdot\ \sqrt{(\omega T_2)^2+1}} \tag{15}$$

The phase relationship is:

$$\phi=90^{\circ}-\tan^{-1}(\omega T_1)-\tan^{-1}(\omega T_2) \tag{16}$$

Equations (15) and (16) present the amplitude ratio and the phase relationship when a velocity signal is used for both the input and the output.

B. Adaptation model

The fundamental assumption is made that the adaptation process involves a short-term homeostatic mechanism which results in a shift of a zero velocity reference level. *Young and Oman* (1969, 1970) assumed that this adaptation mechanism can be represented by a bidirectional process which causes a shift in the reference level by a certain fraction of the time integral of the response itself. If θ_c is the cupular displacement in response to an angular acceleration, the resulting angular eye velocity $(\dot{\theta}_e)$ will be:

$$\dot{\theta}_e(t)=\theta_c(t)- \frac{1}{T_a}\int_0^t \dot{\theta}_e(t)dt \tag{17}$$

where the integral takes account of the shift of the reference level and T_a is the time constant of the adaptation mechanism. Writing:

$$r(t)= \frac{1}{T_a}\ \int_0^t\ \dot{\theta}_e(t)dt, \tag{18}$$

then according to eq.(17):

$$\dot{\theta}_e(t)=\theta_c(t)-r(t) \tag{19}$$

Inserting eq.(19) in eq.(17) gives:

$$\theta_c(t)-r(t)=\theta_c(t)- \frac{1}{T_a}\ \int_0^t\{\theta_c(t)-r(t)\}\ dt$$

Differentiation yields:

$$\frac{d\ r(t)}{dt} = \frac{1}{T_a}\ \{\theta_c(t)-r(t)\} \tag{20}$$

Equations (19) and (20) are the same as those derived by *Malcolm and Melvill Jones* (1970), who made the following assumptions:

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1. the rate of change of the reference level, $r(t)$, is proportional to the value of the difference $\theta_c(t)-r(t)$. Hence $\frac{d\ r(t)}{dt}=b\{\theta_c(t)-r(t)\}$.

2. the eye velocity is proportional to the difference $\theta_c(t)-r(t)$. Hence $\dot{\theta}_e(t) \sim \theta_c(t)-r(t)$.

If eq.(17) is written in Laplace notation, the adaptation transfer function (H_a) can be derived as follows:

$$\dot{\theta}_e(s)=\theta_c(s) - \frac{\dot{\theta}_e(s)}{T_a s}$$

Thus:

$$\dot{\theta}_e(s)\cdot(1+ \frac{1}{T_a s}) = \theta_c(s), \text{ and}$$

$$H_a(s)= \frac{\dot{\theta}_e(s)}{\theta_c(s)} = \frac{1}{1+\dfrac{1}{T_a s}} = \frac{T_a s}{T_a s+1} \qquad (21)$$

C. Second order model with adaptation

Leaving out the gain of the vestibular system the overall transfer function of the second order model of semicircular canal function with an adaptation term can be found by combining equations (7) and (21):

$$H(s)= \frac{\dot{\theta}_e(s)}{\theta_h(s)} = \frac{k}{(T_1 s+1)(T_2 s+1)} \cdot \frac{T_a s}{T_a s+1} \qquad (22)$$

The block diagram of this function is presented in fig. 3.
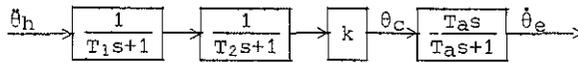
Fig. 3.

This is equivalent to the block diagram of fig. 4.
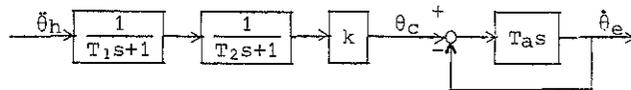
Fig. 4.

1. Response of the second order system with adaptation to an impulse

The transfer function given in eq.(22) can be split up into fractions as follows:

$$\frac{T_a s}{(T_1 s+1)(T_2 s+1)(T_a s+1)} \equiv \frac{A}{T_1 s+1} + \frac{B}{T_2 s+1} + \frac{C}{T_a s+1}$$

A can be calculated by multiplying both sides of this equation by $T_1 s+1$, and inserting $s= - \frac{1}{T_1}$:

$$A= \frac{T_a s(T_1 s+1)}{(T_1 s+1)(T_2 s+1)(T_a s+1)} = \frac{-T_a/T_1}{(-T_2/T_1+1)(-T_a/T_1+1)} = \frac{T_1\cdot T_a}{(T_1-T_2)(T_a-T_1)}$$

B and C can be determined in the same way:

$$B= \frac{T_as(T_2s+1)}{(T_1s+1)(T_2s+1)(T_as+1)} = \frac{-T_a/T_2}{(-T_1/T_2+1)(-T_a/T_2+1)} = \frac{-T_2 \cdot T_a}{(T_1-T_2)(T_a-T_2)}$$

$$C= \frac{T_as(T_as+1)}{(T_1s+1)(T_2s+1)(T_as+1)} = \frac{-1}{(-T_1/T_a+1)(-T_2/T_a+1)} = \frac{-T_a2}{(T_a-T_1)(T_a-T_2)}$$

The second order model with adaptation is thus equivalent to three first order systems connected in parallel, as shown in fig. 5.
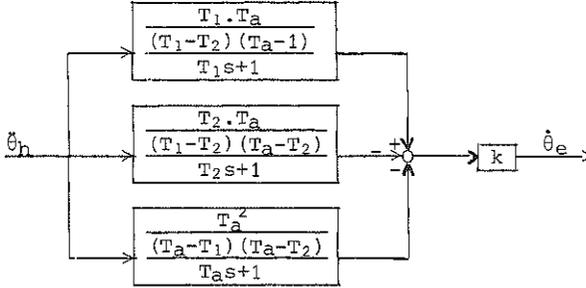

Fig. 5.

The response of the transfer function (22) to a step change in angular velocity is, in the real time domain:

$$\dot{\theta}_e(t)=o \qquad\qquad\qquad\qquad\qquad\qquad \text{for } t=<o$$

$$\dot{\theta}_e(t)=T_1 \cdot T_2 \cdot T_a \left\{ \frac{1}{(T_1-T_2)(T_a-T_1)} \cdot e^{-t/T_1} - \frac{1}{(T_1-T_2)(T_a-T_2)} \cdot e^{-t/T_2} \right.$$

$$\left. - \frac{1}{(T_a-T_1)(T_a-T_2)} \cdot e^{-t/T_a} \right\} \text{ for } t>o$$

Since:

$$\frac{1}{T_a-T_2} - \frac{1}{T_a-T_1} = \frac{(T_a-T_1)-(T_a-T_2)}{(T_a-T_2)(T_a-T_1)} = \frac{-(T_1-T_2)}{(T_a-T_1)(T_a-T_2)}$$

the impulse response can also be written as:

$$\dot{\theta}_e(t)=o \qquad\qquad\qquad\qquad\qquad\qquad \text{for } t=<o$$

$$\dot{\theta}_e(t)= \frac{T_1 \cdot T_2 \cdot T_a}{T_1-T_2} \left\{ \frac{1}{T_a-T_1} \cdot e^{-t/T_1} - \frac{1}{T_a-T_2} \cdot e^{-t/T_2} \right.$$

$$\left. + \left(\frac{1}{T_a-T_2} - \frac{1}{T_a-T_1} \right) \cdot e^{-t/T_a} \right\} \text{ for } t>o \qquad\qquad (23)$$

2. Response of the second order system with adaptation to a step input

The response of the transfer function (22) to unit step acceleration of duration Δt will be, in the real time domain:

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$$\dot\theta_e(t)=o \qquad\qquad\qquad\qquad\qquad\qquad\qquad\text{for } t=<o$$

$$\dot\theta_e(t)= \frac{T_1 \cdot T_2 \cdot T_a}{T_1 - T_2} \left\{ \frac{T_1}{T_a - T_1} (1 - e^{-t/T_1}) - \frac{T_2}{T_a - T_2} (1 - e^{-t/T_2}) \right.$$
$$\left. + (\frac{T_a}{T_a - T_2} - \frac{T_a}{T_a - T_1}) (1 - e^{-t/T_a}) \right\} \text{ for } o < t < \Delta t$$

$$\dot\theta_e(t) = \frac{T_1 \cdot T_2 \cdot T_a}{T_1 - T_2} \left\{ \frac{T_1}{T_a - T_1} (e^{-(t-\Delta t)/T_1} - e^{-t/T_1}) \right. \qquad\qquad (24)$$
$$- \frac{T_2}{T_a - T_2} (e^{-(t-\Delta t)/T_2} - e^{-t/T_2})$$
$$\left. + (\frac{T_a}{T_a - T_2} - \frac{T_a}{T_a - T_1}) (e^{-(t-\Delta t)/T_a} - e^{-t/T_a}) \right\} \text{ for } t > \Delta t$$

3. Response of the second order system with adaptation to a sinusoidal input

The transfer function given in eq.(22) defines the relationship between the output eye velocity ($\dot\theta_e$) and the input head acceleration ($\ddot\theta_h$). If the input acceleration is replaced by the input head velocity ($\dot\theta_h$), the transfer function becomes:

$$H(s) = \frac{\dot\theta_e(s)}{\dot\theta_h(s)} = \frac{T_1 \cdot T_2 \cdot T_a \; s^2}{(T_1 s + 1)(T_2 s + 1)(T_a s + 1)}$$

In the real time domain, the amplitude ratio is:

$$\alpha = \frac{\omega^2 \; T_1 \cdot T_2 \cdot T_a}{\sqrt{(\omega T_1)^2 + 1} \; . \; \sqrt{(\omega T_2)^2 + 1} \; . \; \sqrt{(\omega T_a)^2 + 1}} \qquad\qquad (25)$$

The phase relationship is:

$$\phi = 180^o - \tan^{-1} (\omega T_1) - \tan^{-1} (\omega T_2) - \tan^{-1} (\omega T_a) \qquad\qquad (26)$$

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SUMMARY

In this thesis the influence of adaptation on the response of the
human vestibulo-ocular reflex (VOR) was systematically determined for
three types of stimulation. The stimuli were administered by means of
a room which rotated about the vertical axis. The subject was seated
in a chair in such a way that his head was upright and at the centre
of rotation.

In the general introduction the distinction is made between adapt-
ation and the effects due to habituation and fatigue. As each chapter
was written as a paper, dealing with a specific subject, the descript-
ion of the problems under investigation and the references are contained
within the chapters.

In section I impulsive stimuli were used. The intra- and inter-
subject variance were investigated in chapter I.
    ABSTRACT of chapter I
    The literature on cupulometry shows inconsistent data as to (1)
the magnitude of the time constant T_1; (2) the inter-subject variance;
(3) the difference in T_1 between clockwise and counter-clockwise rotat-
ion, and (4) the linearity of the system. In our investigations, the
nystagmus was measured after a step in angular velocity. All tests
were carried out six times for 5 subjects. The time constant T_1 was
calculated from the slope of the decay of the slow phase eye velocity.
Statistical evaluation of the results showed: an intra-subject variance
which is greater than the inter-subject variance; significant differen-
ces between subjects; mean values of T_1 for clockwise and counter-
clockwise rotation of 13.2 s (SD=1.4 s) and 12.8 s (SD=1.7 s) respect-
ivily; a significant difference of T_1 between clockwise and counter-
clockwise rotations for individual subjects at the 95% confidence inter-
val level; no relation between T_1 and the amplitude of the step in an-
gular velocity, and a linear increase of the maximum slow phase eye
velocity with the amplitude for velocities below 100 °/s, whereas at
higher velocities saturation occurs.

In chapters II and III the influence of the adaptation mechanism
on the long time constant T_1 of the VOR-response was determined
theoretically and experimentally.
    ABSTRACT of chapter II
    From the impulse response of the human vestibulo-ocular reflex
system the value of the long time constant T_1 can be calculated in two
different ways: (a) by plotting the decay of the response on log-
linear graph paper, or (b) by plotting the duration of the response
against the logarithm of the impulse amplitude for various impulse ampli-
tudes, i.e. the cupulometric method. By means of mathematical models,
with and without adaptation, the effect of the two methods of calculat-
ion on the value of the response T_1 was determined. The adaptation
term was demonstrated to give a distinct reduction in the value of the
response T_1 compared with that of the cupular T_1, especially when the
cupulometric method (b) was used. The extent of this reduction was cal-
culated.

ABSTRACT of chapter III
The response of the VOR-system was measured after a start or stop
in angular velocity around the vertical axis. All determinations were
carried out six times for 5 subjects. In a previous study (chapter I)
the mean value of the response T_1 was calculated from the slope of the
decay of the slow phase eye velocity (method a) and found to be 13.2 s
(SD=1.4 s) for CW-stimulation, and 12.8 s (SD=1.7 s) for CCW-stimulation.
Using the cupulometric method (b) with a fixed threshold for the slow
phase eye velocity, these values are 12.1 s (SD=2.0 s) and 11.2 s
(SD=1.4 s) respectively. The difference between the values calculated
by method (a) and those calculated by method (b) is in line with the
theoretical predictions as formulated in the previous chapter (chapter II).

In section II sinusoidal stimulation was used. The theoretical
and experimental frequency responses of the VOR-system were described
in chapters IV and V, and the effect of adaptation was determined at low
frequencies.

ABSTRACT of chapter IV
From the mathematical model of the human VOR-system the frequency
response has been calculated for harmonic sinusoidal acceleration. The
addition of an adaptation term to the second order model, describing the
cupular behaviour, results in considerable changes in the response charac-
teristics in the low frequency region. An attempt has been made to quantify
the influence of the cupular time constant T_1 and the adaptation time
constant T_a on the amplitude and phase characteristics of the transfer
function, which represents the human VOR-system. The results of this
theoretical study will be employed in the following chapter.

ABSTRACT of chapter V
The frequency response of the human VOR-system was investigated by
determining its amplitude and phase characteristics. The angular head
velocity and the resulting angular eye velocity were measured in 7 healthy
subjects using a rotation room. Rotations about a vertical axis were
carried out at frequencies ranging from 0.0025 Hz to 0.1 Hz; peak head
velocity was 50 ^{o}/s. From the experimental data the gain and the phase
relationship were calculated. The results appear to be in agreement with
the frequency response of the theoretical transfer function which repre-
sents the VOR-system. This is based on a second order differential
equation for cupular behaviour, modified by an adaptation term (chapter IV).
According to the experimental phase characteristic the cupular res-
toration time constant T_1 was 16.6 s, and the adaptation time constant
was 114 s. Linearity of the VOR-system, both for amplitude and phase,
was demonstrated at frequencies of 0.05 Hz and 0.005 Hz.

In section III constant angular acceleration was used as a
stimulus. In chapter VI the theoretical response was calculated,
and in chapter VII a small group of subjects showed results which
are not explained by current theory.

ABSTRACT of chapter VI
The response of the human VOR-system to a constant angular acceler-
ation is calculated using a second order model with an adaptation term.
After first reaching a maximum the peracceleratory response declines.
When the stimulus duration is long the decay is mainly governed by the

adaptation time constant T_a, which enables this time constant to be reliably estimated. In the postacceleratory period of constant velocity there is a reversal in response. The magnitude and the time course of the per- and postacceleratory response are calculated for various values of the cupular time constant T_1, the adaptation time constant T_a and the stimulus duration, thus enabling their influence to be assessed.

ABSTRACT of chapter VII

The VOR-response to a constant angular acceleration was investigated in a small group of subjects by varying the stimulus amplitude and the stimulus duration. Various parameters of the response were determined and compared with the results of the theoretical study (chapter VI). This form of stimulation yields a rather high value for the adaptation time constant T_a, which perhaps indicates that there is an adaptation gain of less than unity. This supposition is supported by finding of non-linearity within the VOR-system at high stimulus amplitudes.

Finally, in the general discussion an assessment is made of the extent to which the second order model with adaptation can account for the experimental results, and hence of the extent to which it accounts for the functioning of the VOR-system. This was done by comparing the gain and the values of the time constants T_1 and T_a obtained with the various stimuli.

The appendix contains a comprehensive description of the derivation of the equations used.

SAMENVATTING

Een beweging van het hoofd prikkelt de zintuigen in de halfcir-
kelvormige kanalen van de evenwichtsorganen, hetgeen leidt tot een
oogbeweging in een tegengestelde richting. Dit volledig automatische
proces vindt plaats binnen het vestibulo-oculaire reflex (VOR) systeem.
Het zorgt aldus voor een constante blikrichting en daarmee voor een
stabilisatie van het beeld op het netvlies.

De natuurlijke prikkel voor de zintuigen in de halfcirkelvormige
kanalen is de hoekversnelling. Deze versnelling veroorzaakt, ten ge-
volge van het achterblijven van de vloeistof (endolymphe) in de kanalen,
een uitwijking van de cupula. De uitslag van de cupula prikkelt de
zintuigzenuwcellen die op hun beurt de prikkel overbrengen op de achtste
hersenzenuw. Op deze wijze wordt de prikkel naar de hersenstam geleid,
alwaar overschakeling plaats vindt op de zenuwen naar de oogspieren,
uiteindelijk resulterend in een oogbeweging met een richting tegenover-
gesteld aan die van de versnelling van het hoofd.

Het komt er dus op neer dat een hoekversnelling (in $\circ/s^2$) een
uitslag (in graden) van de cupula veroorzaakt, waardoor een oogsnelheid
(in $\circ/s$) in tegengestelde richting ontstaat.

Op grond van de mechanica van het cupula-endolymphe-systeem is
omstreeks 1930 een mathematisch model opgesteld, waarmee de cupula-
uitslag voor een bepaalde hoekversnelling berekend kan worden. Indien
de resulterende oogsnelheid evenredig verondersteld wordt met de cu-
pula-uitslag, dan zou met dit zogenaamde 2e orde model de overdrachts-
functie van het VOR-systeem bepaald zijn.

Tijdens onderzoek aan het VOR-systeem bleek echter dat de resul-
taten niet geheel klopten met de voorspellingen die gedaan waren op
grond van het 2e orde model. Bij een langdurige stimulatie nam de
reactie van het VOR-systeem langzaam af (adaptatie). Om deze afname
te kunnen beschrijven werd omstreeks 1970 een adaptatie-term aan het
2e orde model toegevoegd.

In dit proefschrift zijn de reacties van het 2e orde model met
en zonder adaptatie systematisch onderzocht voor drie verschillende
vormen van hoekversnelling. Tevens zijn de reacties van het VOR-sy-
steem op dezelfde vormen van versnelling bij enkele gezonde proefper-
sonen bepaald en vergeleken met de voorspellingen, gedaan op grond
van de uitkomsten uit de theoretische berekeningen.

In sectie I is als stimulus een impuls gebruikt. Deze vorm
van versnelling werd verkregen door een plotselinge verandering in de
draaisnelheid om de verticale as van een proefpersoon. De reacties
van het 2e orde model zonder adaptatie, dat wil zeggen de cupula-
uitslag (θ_c), en die van het 2e orde model met adaptatie, dat wil
zeggen de resulterende oogsnelheid $(\dot{\theta}_e)$ staan weergegeven in fig. 1.
De toevoeging van de adaptatieterm veroorzaakt een snellere afname
en een omkering van richting van de oogsnelheid in de periode volgend
op de impuls. Deze verschijnselen werden bij alle proefpersonen gevon-
den.
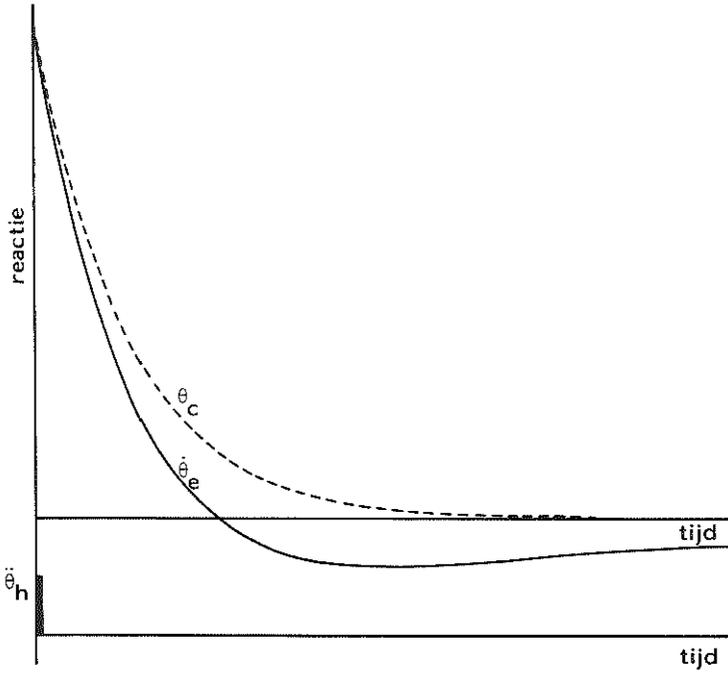
Fig. 1. Reactie van het 2e orde model zonder (onderbroken lijn) en met adaptatie (ononderbroken lijn) op een impulsvormige stimulus. θ_c=uitslag van de cupula; $\dot{\theta}_e$=snelheid van het oog en $\ddot{\theta}_h$=versnelling van het hoofd.
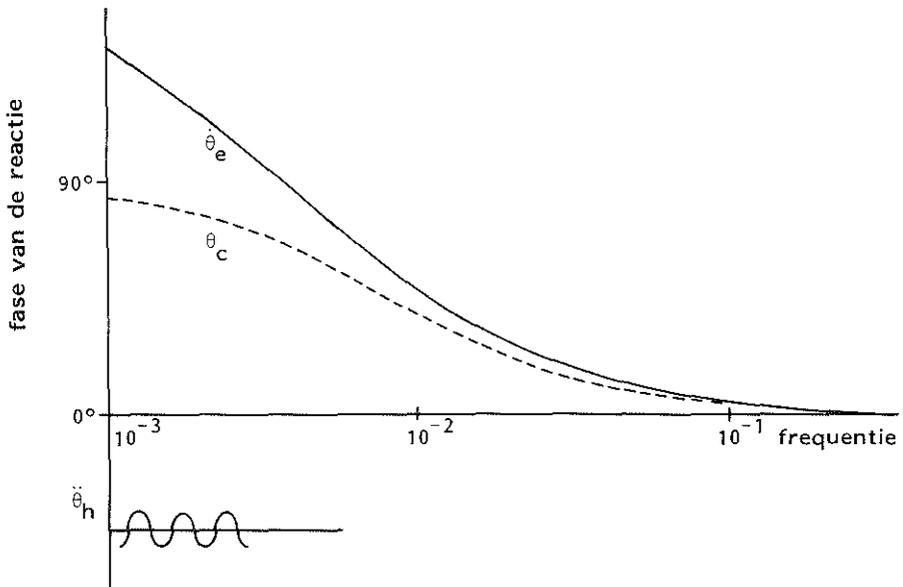
Fig. 2. Fase-voorloop van het 2e orde model zonder (onderbroken lijn) en met adaptatie (ononderbroken lijn). θ_c=fase van de cupula-uitslag; $\dot{\theta}_e$=fase van de oogsnelheid. θ_c en $\dot{\theta}_e$ zijn berekend ten opzichte van de fase van de hoofdsnelheid.
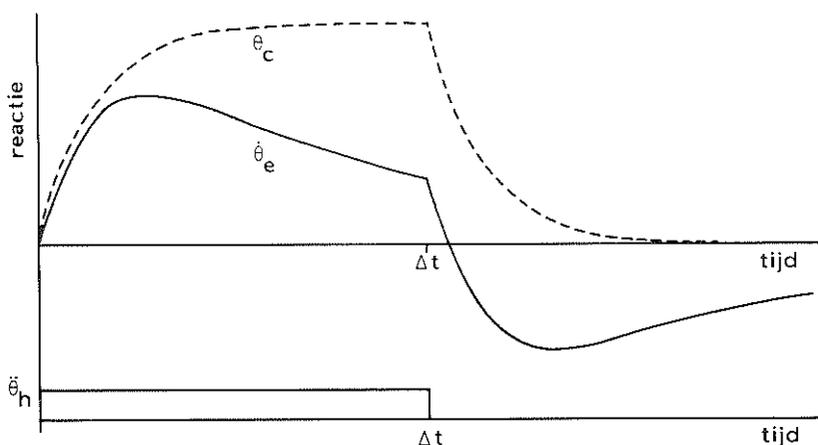
*Fig. 3. Reactie van het 2e orde model zonder (onderbroken lijn)
en met adaptatie (ononderbroken lijn) tijdens en na een periode met
constante versnelling. θ_c=uitslag van de cupula; $\dot{\theta}_e$=snelheid van
het oog en $\ddot{\theta}_h$=versnelling van het hoofd.*

      In sectie II is de sinusvormige versnelling als prikkel toegepast.
De fase van de oogsnelheid en de hoofdsnelheid zijn met elkaar verge-
leken voor verschillende frequenties. In fig. 2 staan de resultaten
van de theoretische berekeningen weergegeven. De fase van de cupula-
uitslag (θ_c) blijkt maximaal 90 graden voor te lopen. De toevoeging
van de adaptatie-term resulteert in een grotere fase-voorloop van
de oogsnelheid ($\dot{\theta}_e$). Een fase-voorloop van meer dan 90 graden, optre-
dend in de lage frequenties, werd bij alle proefpersonen aangetoond.

      In sectie III is een langdurige, constante versnelling gebruikt.
De cupula-uitslag (θ_c) blijkt in de periode van constante versnelling
een eindwaarde te bereiken, terwijl de oogsnelheid ($\dot{\theta}_e$) na een maximum
afneemt (fig. 3). Dit laatste werd ook gevonden bij het onderzoek van
de reacties van het VOR-systeem bij enkele gezonde proefpersonen.

      Op grond van dit onderzoek kan gesteld worden dat het 2e orde
model met een adaptatie-term een goede voorspelling geeft van de reac-
ties van het vestibulo-oculaire reflex-systeem van de mens.

CURRICULUM VITAE

The author was born in 1946 in Nijmegen. Raised and educated there, he obtained his Gymnasium β from St.Canisius College and qualified at the University of Nijmegen in 1972. After Military Service as a Medical Officer, he worked at the Pieter Pauw Hospital, Wageningen, first as assistent-surgeon and later as an ENT-assistent. In 1977 he accepted an appointment as Clinical Assistent in ENT at the University Hospital Dijkzigt, Rotterdam. He was registered as an ENT specialist in 1981. The author currently practises in the ENT departments of 2 hospitals in Rotterdam, Dijkzigt and Zuiderziekenhuis. All the work for this thesis was carried out at Erasmus University, Rotterdam. The author is married and has a family of three daugthers.