

European vestibular experiments on the Spacelab-1 mission: 3. Caloric nystagmus in microgravity

H. Scherer¹, U. Brandt², A. H. Clarke^{1*}, U. Merbold³, and R. Parker⁴

¹ Institut für Otolaryngology, Klinikum Großhadern, Universität München, D-8000 München, Federal Republic of Germany ² Swedish Air Force (retired); ³ SL1 Payload Specialist, ESA; ⁴ SL1 Mission Specialist, NASA

Summary. Response to caloric stimulation was examined in two subjects in the weightless environment of orbital flight. Using air insufflation, a binaural temperature stimulus profile was performed twice on each subject during flight. In all but one test, which was carried out on the first mission day, a caloric nystagmus was registered. This zero-g nystagmus was similar to ground-based pre- and postflight responses with regard to its intensity, its temporal correlation with the stimulus profile (nystagmus was always directed towards the warmer ear) and the subjective sensations reported by the tested subjects. These findings demonstrate that mechanisms other than thermoconvection are involved in the elicitation of the caloric nystagmus response. At each stage of the temperature stimulus profile, linear acceleratory stimulation was presented in the form of oscillations in the X-axis. Some differences were found between one-g and zero-g conditions in the resultant modification of the nystagmus response.

Key words: Caloric stimulation – Microgravity – Nystagmus – Bárány – Spacelab 1 – Orbital flight

Introduction

The caloric experiment carried out during the Spacelab SL1 mission was designed to examine the adequacy of the thermoconvection model of the caloric mechanism, and to examine the interaction between the signals from the otolith and semicircular canal organs.

Since its initial publication by Bárány (1906), this explanation of the caloric nystagmus, based on a

thermo-convective peripheral mechanism has, despite some objections, remained largely acceptable to the majority of the vestibular community. It should be made clear at this point that regardless of the true nature of the peripheral mechanism, the caloric test – which involves non-physiological stimulation of the individual vestibular organs – remains central to the clinical examination of vestibular disorders, as it has done since its introduction by Bárány.

According to the convection theory the temperature gradient within the temporal bone, produced by irrigation with water at temperatures above or below body temperature, causes circulation of the endolymph within the membraneous duct by thermal convection. In the meantime, however, it has been established that the cupula occludes the lumen of the ampulla and thus the endolymph is not free to circulate around the semicircular duct. Consequently, the theory of convective flow has been modified such that during caloric stimulation the anisotropic changes in endolymph density caused by the temperature gradient across the plane of the semicircular canal duct are said to produce a convective torque, which can be expressed as a differential pressure across the cupula (Steer 1967; Oman and Young 1969).

Under conditions of microgravity, as are prevalent in Spacelab during orbital flight, no thermoconvective effect may occur. Thus, according to the theory of Bárány, no corresponding stimulation of the semicircular canal receptors should result during the caloric test. This has been supported by a number of researchers, for example by Bergstedt (1961), who, extrapolating from centrifuge measurements involving accelerations upwards of one-g, predicted that in zero-g conditions the caloric reaction should disappear. In a study involving caloric stimulation during parabolic flight, Oosterveld and van der

^{*} Dr. Clarke collaborated during data evaluation

Offprint requests to: H. Scherer (address see above)





Laarse (1969) reported the immediate disappearance of nystagmus response on entry into zero-g acceleration. The authors interpreted these findings as verification of the convection hypothesis. In a more extensive parabolic flight experiment, Graybiel et al. (1980) observed a similar disappearance of what they termed the primary nystagmus. During the zero-g episodes, however, they measured an opposite-beating secondary nystagmus.

It was one aim of the present experiment to exploit the longer-term zero-g conditions in Spacelab to resolve this matter and to determine whether any other mechanisms could be responsible for elicitation of a caloric response.

A further aim of the experiment was to examine the response of the vestibular system when both the semicircular canals and the otolith organs are stimulated under controlled conditions in the hypogravic range, free of the predominant one-g vector as on Earth.

Interaction between the signals from the otolith and canal organs has been discussed by a number of authors (e.g. Fluur and Siegborn 1973; Benson 1974; Baloh and Honrubia 1979; von Baumgarten et al. 1980; Schmidt 1985). However, behavioural evidence remains circumstantial and the issue has yet to be resolved.

Method

Caloric stimulation was presented by means of air insufflation. The safety restrictions in the zero-g environment in Spacelab precluded the use of the more common water irrigation. The temperature of the air was regulated by Peltier elements which were electronically regulated to deliver air temperature of between 15° C and 44° C to each ear. Ultimate temperature sensors were positioned in the ear tubes directly at the entrance to the external auditory canals.

The stimulation technique employed for the experimental measurements was developed specially for the Spacelab environment. The validity of the technique was tested exhaustively during early crew training. The apparatus permits the individual selection of the desired stimulus temperature pairs, which are then regulated under programmed control. The stimulus profile used is illustrated in Fig. 1.

Both ears were stimulated simultaneously, one ear with air above and the other with air below body temperature. This stimulus mode was employed to increase the intrinsically lower effective intensity of stimulation obtained with air insufflation than with water irrigation, and further to simulate the bilateral stimulus configuration produced by rotational acceleration.

As can be seen from the stimulus profile (Fig. 1), the temperature gradient was reversed after reaching the highest level of 44° R – 15° L. At each differential temperature in the profile, the subject remained stationary for two minutes (static phase). Thereafter, the subject was accelerated back and forward whilst sitting in the upright position (X-axis). Six cycles of back and forward movements of 6 resp. 3 s duration were performed. The computer-controlled sled which had been designed for this phase was not flown on the SL1 mission, so that the inflight linear acceleration stimuli had to be generated by manual oscillation, the subject being seated in a body restraint system (BRS). The amplitude of the linear movement was approximately 70 to 80 cm. Pre- and postflight linear acceleration tests were performed with the NASA sled in Kennedy Space Center. The sled run length was 8 m. Acceleration was recorded by a triaxial accelerometer system mounted on the vestibular helmet. Horizontal and vertical eye movements were recorded using standard electrooculographic (EOG) electrode placements - monocular horizontal and vertical, and by means of the specially developed infrared video camera system EMIR which enabled online digital processing of horizontal and vertical eye movements (see Kass et al. 1985, this issue, for details of the equipment).

With the exception of the dynamic phase, the preflight, inflight and postflight test procedures were identical. The caloric experiment was carried out with two test subjects C and D. Preflight measurements were carried out on both subjects on day $F-30^1$. Subject C was tested on inflight days F2 and F7, subject D on inflight days F0 and F8. Both subjects were tested postflight on days R+1, R+2 and R+6. To date, the results from days R+1 and R+2 have been available for analysis.

¹ For the peflight period, days are numbered with reference to the day when the mission started, thus F-30 was thirty days before mission; during mission the days are numbered from F0 (zero) onwards; postflight they are numbered from the day of return R+1, R+2 etc. onwards



Fig. 2a-d. Examples of recorded horizontal eye movements: Subject D. a Preflight (F-30), stimulus 15° R-44° L (EOG). b Inflight (F0), stimulus 44° R-15° L (EMIR). c Inflight (F8), stimulus 15° R-44° L (EMIR). d Inflight (F8), stimulus 44° R-20° L (EOG). The examples in c and d illustrate nystagmus inversion during inflight testing

Note: eye movements to the right are represented by upward deflection

Further ground tests were made on both subjects fourteen months after the mission to investigate body-position modification of the nystagmus intensity.

Data analysis

The horizontal EOG and EMIR traces from the polygraph recordings were used to evaluate the nystagmus activity. The slow phase velocity (SPV) of the horizontal nystagmus, measured in degrees/second, represented the primary measure of the nystagmus intensity. Due to artefacts from a number of sources, continuous automatic EOG analysis was not considered practicable. Slow phase velocity (SPV) of nystagmus was measured for those periods during which nystagmus beats were clearly recognisable. Analysis of the results of the dynamic phase measurements involved evaluation of each recognisable nystagmus beat. If, as hypothesised, a modification of the nystagmus activity occurs during linear acceleration, this should be reflected in the nystagmus response as averaged against the linear oscillatory stimulus. A technique was employed, by which the responses over each complete oscillatory cycle were averaged.

Results

Subject D

During preflight testing on day F-30 (Figs. 2a, 3a), a nystagmus intensity of up to 25 deg/s SPV right and left was elicited during the maximum stimulus stages $(44^{\circ} R - 15^{\circ} L \text{ resp. } 15^{\circ} R - 44^{\circ} L)$. During the first inflight test, on day F0, no discernible nystagmus was observed. During maximum stimulation (44° R -15° L) only a few nystagmus patterns were found in the horizontal EOG whose validity remains doubtful. The subject did not report any sensations such as normally accompany caloric stimulation. The EOG recordings were rather characterised by large amplitude, slow frequency eye movements (Fig. 2b) typically observed in tired subjects, and the drooping eyelids, shown by the video image (EMIR) of the eye showed clearly the subject's reduced level of vigilance. However, even during those periods when the subject could be kept alert by occupation with mental tasks, no notable nystagmus response was recorded. Subject D was tested again on mission day 8. The horizontal EOG recorded exhibited strong nystagmus response both to the right and to the left (Fig. 2c, d), the direction being towards the warmer ear (Fig. 3b). The intensity of the left beating nystagmus was observed to exceed 40 deg/s, a stronger response than during baseline measurement.

This test was commenced with a differential temperature of $\Delta T = 12 \text{ C}^{\circ}$. Even at this low stimulus intensity a prompt nystagmus response was elicited.

From the postflight measurements performed on day R+1, 24 hours after landing (Fig. 3c), it can be observed that the intensity of the response is comparable to preflight (F-30) and day F8 inflight.

All ground-based tests were performed with the head of both subjects in the upright position (i.e. Z-axis of head aligned with gravitational vertical). For this reason additional baseline tests were conducted to establish any difference in the caloric response due to body position. Measurements were made in the position such that the plane of the lateral semicircular canals was in line with the Earth's gravitational vertical (30° -optimum) and in the upright (90°) position as in all other ground tests. The results of this test indicated that the nystagmus intensity was 25%



Fig. 3a-c.² Subject D. Nystagmus intensity (SPV, full line) and differential temperature profile (ΔT , dashed line) versus elapsed time as measured a Preflight F-30, b Inflight F8 and c Postflight R+1

greater in the 30° optimum position than in the 90 upright position.

Subject C

In the preflight baseline testing on day F-30 (Fig. 5a) a maximum response of ca. 5 deg/s was measured.

During the first mission test on day F2 the polygraph recording exhibited a substantial amount of artefact (Fig. 4a), such that only the EMIR signals were of use for evaluation. During maximum stimulation $(44^{\circ} R - 15^{\circ} L)$ a nystagmus response in both directions was measured (Fig. 5b), although it was weaker than during baseline tests. During the second inflight test on day F7 a clear nystagmus response (Fig. 4b) was recorded having an overall response (Fig. 5c) greater than that measured on day F2 and, in general, comparable to that recorded preflight.

² In order to simplify the figures, differential temperature gradients (ΔT_{r-1}) are plotted rather than the individual ear temperature trajectories

During postflight measurement on day R+1, the rightbeating nystagmus was slightly less than preflight, whereas the intensity of the leftbeating nystagmus intensity was comparable (Figs. 4d, 5d). During the second postflight measurement on day R+2, the overall response was comparable to preflight.

The results of the additional ground tests for examining the effect of body position yielded a reduction of 40% in nystagmus intensity from the 30° optimum to the 90° upright position.

During the ground-based tests and the second inflight (F7) test, occasional rotatory eye movements were observed on the EMIR video image of the subject's eye. However, no quantitative evaluation of this component has as yet been possible.

Dynamic stimulation

Examples of the cycle-by-cycle averaged response from pre-, in- and postflight dynamic phase measurements are presented in Fig. 6. It appears that, as reflected in the averaged response, no recognisable modification of nystagmus activity during groundbased tests is present. However, the response calculated for the inflight data would indicate that nystagmus beats occur predominantly during intervals of positive going acceleration.

Latency measurements

Latency of nystagmus onset can in principle be measured at the beginning of the experiment, when the insufflation stimulus is commenced, and after the temperature turnover points midway through the stimulus profile. However, it proved difficult to measure onset latency at the start of the temperature profiles due to

a) the low stimulus intensity in the first stage of the profile, during which very little nystagmus activity was observed, and

b) the presence of artefact.

Both of these factors made difficult any reliable recognition of the first nystagmus beats.

Nevertheless, for subject D, it can be observed (Fig. 3) that the latency of nystagmus onset during inflight testing was comparable to that measured preand postflight. In the case of subject C it was found that in early flight, onset was somewhat later than pre- and postflight, whereas during the second inflight test on day F7, the latency was again comparable.



Fig. 4a–d. Examples of horizontal eye movement records: Subject C. Note: eye movements to the right are represented as upward deflection. a Inflight F2, stimulus 15° R–44° L (EMIR), b Inflight F7, stimulus 15° R–44° L (EOG), c Inflight F7, stimulus 44° R–15° L (EOG), d Postflight R+2, stimulus 44° R–15° L (EOG)

In addition, it was possible to measure the latency of nystagmus reversal after the stimulus temperature turnover from 44° R – 15° L to 20° R – 44° L. Clear ongoing nystagmus beats to the right were seen before the temperature change, followed by leftbeating nystagmus some time after the new stimulus temperature pair were established. Latency of nystagmus reversal was defined as the interval between obtaining 0° C differential temperature between outer ear canals and the onset of the first leftbeating nystagmus. The results of the measurements are shown in Table 1. It can be seen that inflight latencies at the temperature turnover point appear to be longer than those measured pre- and postflight.



Fig. 5a-d. Subject C. Nystagmus intensity (SPV) and differential temperature gradient between ears (ΔT) against elapsed time for tests performed on a preflight F-30, b inflight F2, c inflight F7, d postflight R+1



Fig. 6A–C. Responses to linear acceleration: The figure illustrates the occurrence of nystagmus beats as averaged over the linear oscillatory cycle. Subject C: A preflight F-30, stimulus 15°R–44° L, B inflight F7, stimulus 15° R–44° L, C postflight R+1, stimulus 15° R–44° L

Discussion

During the zero-g conditions of orbital flight a caloric nystagmus could be elicited in both tested subjects. As on Earth, this zero-g nystagmus was directed consistently to the warmer ear and was reversed after inverting the temperature gradient between ears. It was found that in all cases except day F0, on which no nystagmus was observed in the tested subject, the nystagmus response correlated with the stimulus trajectory.

Table 1. Latencies of nystagmus inversion after temperature turnover. Latency was defined as the interval between arrival at zero differential temperature ($\Delta T = 0$) and appearance of first nystagmus beats to the opposite side (left)

Subject D	Day Number Latency (s)	F-30 53	F8 74	R+1 63		
Subject C	Day Number	F-30	F2	F7	R +1	R+2
	Latency (s)	81	107	103	68	69

Although much evidence has been published in support of the convection model, various recent findings point to possible discrepancies. Of particular interest is the research of Coats and Smith (1967) on the relationship between the caloric nystagmus response and the orientation of the labyrinth to the Earth's gravitational vertical. In agreement with earlier findings (Veits 1928; Behrmann 1940) these authors found that the maximum face-up response was greater than the maximum face-down response. According to the convection model, the response intensity should be symmetrical through the face-up and face-down ranges of body positions. Coats and Smith (1967) discuss various possible mechanisms to explain this discrepancy, favouring the idea of a secondary gravity-independent mechanism. During orbital flight it is not possible to produce a constant g-vector as on Earth, so that the issue of bodyposition becomes irrelevant. Thus, testing of any body-positional modification is excluded in zero-g conditions.

Although no precise measurement of onset latency was possible, comparable behaviour was observed in the one-g and zero-g conditions. Latency of nystagmus reversal, on the other hand, appeared to be slightly longer under zero-g conditions. However, due to the limitations of the space environment the measurement resolution possible with the available data remains very coarse and these findings must be treated with caution.

Subject D

On day 0 of the mission, no nystagmus was observed, either in the EOG record or on the video image of the eye (EMIR) transmitted to ground during the vestibular experiments. The large amplitude, slow frequency eye movements which were recorded indicated rather the reduced state of vigilance in the subject. The subject also reported difficulty in staying awake and keeping his eyes open. This subject was premedicated with antivertiginous drugs which are known to have a sedative side effect. This alone could explain the failure of nystagmus to appear. Nevertheless, even during those periods of alertness obtained by presentation of mental tasks, there was no observable nystagmus response. However, the presence of a well-defined response to thermal stimulation later in the mission lends some support to the idea that the transient failure to elicit nystagmus during early flight might be due to some extent to a change in the weighting of the afferent signals from the otolithic receptors; this being part of the adaptive process consequent to transfer from one-g to zero-g conditions.

In contrast to day F0, the test results from day F8 exhibit a distinct nystagmus response. Both its intensity and its correlation with the temperature trajectory corresponded closely with the results obtained preflight. Indeed, the left nystagmus was stronger than that measured preflight. By day F8 subject D was free of medication and could be considered as adapted to zero-g conditions. Thus, these two possible sources for nystagmus response failure on day 0namely, sedative effect of drugs and initial adaptative processes – can both be excluded on day F8. At present it cannot be determined with any degree of certainty to what extent either of these factors were responsible for the absence of nystagmus in subject D on day F0.

The postflight data available from day R+1 are similar to those recorded preflight and inflight on day F8 in intensity and correlation with temperature profile.

Subject C

The absolute intensity of this subject's response was lower than that of subject D. This can be attributed to the large interindividual variability in the caloric response (Baloh and Honrubia 1979). The preflight baseline test yielded a normal nystagmus response with respect to intensity and correlation with the stimulus trajectory. On both inflight days tested, a caloric nystagmus response was elicited. It is notable that the intensity of the first inflight response was somewhat weaker than baseline, whereas the second inflight response can be considered comparable. This increase of response over the course of the mission cannot be accounted for by drug-induced sedation; this subject was free of medication for both inflight tests. Thus, this finding would lend support to the idea that a central adaptative mechanism be responsible for the modification of the nystagmus intensity during the course of the mission. The postflight data recorded on days R+1 and R+2 also correspond in intensity and trajectory with those from preflight and inflight day F7.

Dynamic stimulation

Modification of the nystagmus response originating from the stimulation of the semicircular canals may be attributed to either a central interaction with the signals from the otolithic receptors, which register any linear acceleration, or possibly to a direct fluidmechanical influence on the endolymph in the lateral semicircular canals. In this sense, the linear acceleration would create a g-vector component parallel to the plane of the lateral semicircular canal and thus enable the development of a convective torque.

The observed influence of linear acceleratory stimulation on nystagmus occurrence in zero-g conditions would accord with previous findings of central interaction between the signals from the semicircular canals and the otolith organs (Owada and Okuno 1963; Milojewic and Voots 1966; Barnes and Benson 1978). These authors reported that linear acceleration had the effect of extending the nystagmus response.

A further parallel may perhaps be drawn between the present findings and those of Buizza et al. (1980) who observed an otolithic modification of the optokinetic nystagmus, and who proposed a model based on control theory for the effect.

Whatever the mechanism involved, the present results indicate that rate of change of the acceleration vector plays the essential role, i.e. nystagmus is enhanced during positive-changing acceleration and suppressed during negative-changing acceleration. The experiments planned for the next European Spacelab mission, which will include linear acceleratory stimulation with a programmed sled, promise more precise stimulus control and more reliable data.

Effect of body position

The pre- and postflight ground measurements were all performed with the subjects' heads in an upright (90°) position. According to the sinusoid model of Coats and Smith (1967) this would correspond to a 60° deviation from the optimum response position of 30°, therefore implying an expected 50% reduction in nystagmus response (sin 60°) with respect to the optimum possible in the one-g conditions prevalent during ground tests. On inspection of Coats and Smith's (1967) published experimental data, it can be noted that a large interindividual variability can be seen over the range between 0° and 90° for those subjects tested in all measurement positions. This has been confirmed in an unpublished study performed in our laboratory. Accordingly, it cannot be assumed that the theoretical 30° maximum necessarily applies

to the subjects examined here. The results from additional ground testing demonstrated a reduction in response from the 30° to the 90° position of 40% in subject C and 25% in subject D. This must be considered together with the other findings. For the present, it will be assumed that both thermoconvective and non-thermoconvective mechanisms contribute to the elicitation of the caloric response.

Thus, on the one hand, the results indicate that the caloric response does not differ substantially between zero-g and one-g in the 90° upright position. Assuming a strictly additive relationship between the thermoconvective and non-thermoconvective mechanisms, this would suggest that the thermoconvective component plays a very minor role. On the other hand, a clear difference does exist between the one-g, upright and one-g, 30° optimum position. This would indicate that the thermoconvective component, which would be modified by body position, is of comparable magnitude to the non-thermoconvective component.

A solution to these seemingly contradictory findings is offered by the introduction of an additional modifying effect, which results from interaction in the central vestibular system between the otolith signals, which also reflect body position with respect to the gravitational vector (Lowenstein and Roberts 1950), and the signals of the semicircular canals. Such an effect could be related to the concept of adaptive coupling described by Benson (1974).

Consideration of the various mechanisms which could be responsible for the space nystagmus and further discussion of a central interaction amongst the labyrinth signals is presented elsewhere (Scherer and Clarke 1985).

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