A new light on caloric test

-What was disclosed by three dimensional analysis of caloric nystagmus?-

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Abstract For better understanding of caloric nystagmus, this phenomenon will be reviewed historically in three stages. **1) The first light** on caloric nystagmus was thrown by Bárány 1906. Through direct observation of eye movements, Bárány established the "caloric test" as an important tool to determine the side of lesion for vertigo. **2) The second light** is shed by electrooculogram (EOG) from the late 1950th. EOG enabled qualitative analysis of caloric nystagmus, and proved Bárány's convection theory, but resulted in neglect of vertical and roll eye movements. **3) The third light is gained by 3D recording of eye movements** started from the late 1980th. 3D recordings of eye movements enabled us to analyze the spatial orientation of caloric nystagmus, and disclose the close correlation of the nystagmus components in the head vertical and the space vertical planes, suggesting a contribution of the velocity storage integrator. The 3D property of caloric nystagmus will be explained in detail.

Key words; caloric nystagmus, gravity, velocity storage, canal plugging, maccaca monkey

For better understanding of caloric nystagmus, this will be reviewed historically in three stages.

1) The first light on caloric nystagmus was thrown by Barany

Robert Bárány, a Nobel Prize Winner, described caloric nystagmus thoroughly in the historical paper, as follows; "..... when the right ear was irrigated with cold water in the right side-down position, this induced mainly rotatory associated with horizontal nystagmus to the left. If the top of the head was tilted on the left shoulder, then the nystagmus was purely horizontal to the right....." (Bárány 1906). Bárány emphasized the physiological mechanism of caloric nystagmus as the convection flow of the endolymph in the lateral semicircular canal. He established the "caloric test" as one of the most important vestibular examination for diagnosing the cause of vertigo, through direct observation of eye movements after caloric stimulation. The caloric nystagmus was described by the duration and the beating direction of the quick phase of nystagmus in three dimensions (3D); horizontal, vertical and roll component with respect to the subject's view.

2) The second light on caloric nystagmus was EOG

In the late 1950th, electrooculogram (EOG) was introduced and has been the most important tool in analyzing caloric nystagmus. EOG allows objective and qualitative analysis of caloric nystagmus, by measuring the slow phase

eye velocity, which corresponds to the excitability of end organs to caloric stimuli (Koibuchi 1978). A huge amount of clinical and basic data has been accumulated. One of the best examples is the proof of Bárány's convection theory by Coats and Smith (Coats and Smith 1967). They recorded caloric nystagmus every 30 degrees in the sagittal plane for 360 degrees from five normal subjects. The maximum slow phase velocities changed in a sine function with regard to head position relative to gravity and the plus/minus maximum was the lateral canal's perpendicular position to the earth. These indicate convection current in the lateral semicircular canal of the stimulated ear.

Since the introduction of EOG, we have almost forgotten the 3D property of caloric nystagmus. The reason is that although EOG provides objective and reliable data of caloric nystagmus, it is limited mainly to the horizontal eye movements. For diagnostic purposes, we record caloric nystagmus to measure slow phase velocity of horizontal nystagmus induced by caloric stimulation in one ear and compare the data to the other ear or normal group. We are used to record caloric nystagmus with eyes open in darkness or with eyes closed, because light and vision suppress caloric nystagmus. Using EOG, we need not look at eye movements. Even when EOG registered vertical nystagmus, we usually neglect it. We had a quarter century of quiet time, until the first European space-mission revealed active caloric nystagmus in micro-gravity as on earth (Von Baumgarten *et al.* 1984). Scherer *et al.* (1985) showed horizontal caloric nystagmus before, during and after the mission, which was elicited by air inflation to the external ear canal, cold in one ear and hot in the other ear. The physiological basis of caloric nystagmus tied down, or there might be different mechanism to cope with the new environment in the space. In the space lab, it is obvious that no convection current occurs during calorization. Also

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in space lab experiments, there was a few days time lag before active caloric nystagmus was recorded.

3) The third light on caloric nystagmus is gained by 3D recording of eye movements.

Then we got the third light; three dimensional recording and analysis of eye movements. A dual search coil system in a uniform electro-magnetic field enabled us to record eye movements in three dimensions. Hot discussion at the Bárány meeting in 1986 turned out into a book "Representation of three-dimensional space in the vestibular, oculomotor, and visual systems" (1988). The cover features the stereo-picture of the labyrinth from a 100 year-old book "The Labyrinth of animals" by Gray (Henn 1988). We are again able to stand the point of 100 years ago.

i) Direction of caloric first phase in 3D

The first description of caloric nystagmus with 3D-eye recording in rhesus monkeys was reported in 1990 (Arai *et al* 1990). The test animals were positioned stereotactically with the lateral semicircular canals laying perpendicular to the earth. Caloric stimulus was given by irrigating 5ml of water at 20 degrees to the external ear canal. Eye movements in total darkness were recorded using a dual search coil system that allowed precise analysis of eye velocity in 3D. The horizontal component (HOR) by the right-ear irrigation in supine position was quick phase to the left. The direction was reversed in prone, and was also reversed by left ear irrigation (Fig. 1a). These directions of nystagmus are identical to those of normal human caloric

nystagmus recorded by EOG.

The vertical component (VER) depended on the position, and not on the ear. The quick phase of VER was to the upper eyelids (up) when supine, and to the lower eyelids (down) when prone (Fig. 1b). Vertical caloric nystagmus in humans has been regarded as pathological "perverted nystagmus". Kawachi (1992), however, carefully examined the EOG of normal human subjects. She found that the pseudo-vertical component recorded by the vertical leads from the right and left eyes in EOG was symmetrical. Considering the pseudo-vertical component, she concluded that the vertical component of caloric nystagmus in normal humans is in the same direction as monkeys. Tsuchiya measured the vertical component of 20 normal human subjects by electrically canceling the pseudo-vertical component, and reported the vertical component as 26% of the horizontal component (6.3 deg/sec in average) in supine (Tsuchiya 1995).

The roll component (ROLL) is ear-dependent; cold calorization to the right ear induces caloric nystagmus quick phase to the right (CW from the subject's view), left ear irrigation induces a quick phase to the left (CCW) independent of head position (Fig. 1c). The roll component was so strong in rhesus monkeys that I could hardly believe the recordings without verifying the eye movements. I confirmed these strong roll eye movements by infrared video movies in rhesus and Japanese monkeys. During clinical EOG examinations, we also observed the movement of one eye using infrared video camera. In human calorization, roll eye movement was recognized in the same direction in half of the patients who were tested

Fig. 1 Velocity traces of horizontal (a), vertical (b) and roll (c) components of caloric nystagmus from a rhesus monkey.

From the first to the fourth row, right-ear irrigation in supine position, right-ear irrigation in prone, left-ear irrigation in supine, and left-ear irrigation in prone position respectively. The whole trace is 3 minutes and upward deflection is right, down, and counterclockwise from the animal's view. The calibration bars indicate 100°/s.

nystagmus stimulation		HOR		VER		ROLL	
supine	R-ear	against the ear	left	facing direction	up	to the ear	CW
	L-ear	against the ear	right	facing direction	up	to the ear	CCW
prone	R-ear	to the ear	left	facing direction	down	to the ear	CW
	L-ear	to the ear	right	facing direction	down	to the ear	CCW

routinely. In the remaining half, the roll component was hardly detectable, but none showed the opposite direction.

So, we assume that caloric nystagmus in monkeys and humans are beating in the same direction three-dimensionally.

ii) Direction of caloric second phase

It was remarkable that the ROLL second phase was also very strong and long lasting. At the peak of the second phase, I tried to turn the primate chair 90 degrees in the dark. For example, by right ear calorization in prone position, the second phase was CCW and was repeatable. I then turned the chair 90 degrees to bring the monkey in right-ear-up position. Then, the predominantly roll nystagmus changed to vertical nystagmus (Fig. 2).

This might indicate gravity dependent nature of the second phase. We seldom record caloric second phase in human examination, perhaps because we keep the subjects in supine, and observe horizontal instead of roll eye movements using EOG. If we change the position by 90 degrees from supine to the upright, then second phase nystagmus may be recorded by EOG. In a routine caloric test, I brought the patient upright when the caloric nystagmus was completed. All of the patients who elicited

caloric nystagmus showed horizontal nystagmus opposite to the caloric first phase. This nystagmus is considered as identical to the caloric second phase.

Thereafter, I systematically tested in rhesus monkeys the effect of gravity to the caloric second phase (Arai *et al* 1991).

Caloric first phase was recorded either in supine or prone position, and the irrigation was given either to the right or to the left ear. When the second phase almost reached the peak, the position was changed 90 degrees, either to upright, right-ear-down or right-ear-up. By the right ear cold stimulation in prone position, the strongest component among the three was always to CCW. The strongest component of the caloric second phase changed to left in upright position, changed to up (upper eye lid) in the right-ear-up side position, and changed to down (lower eye lid) in the right-ear-down position. In other words, the strongest component of the caloric second phase changed according to the head position in head fixed expression (Fig. 3 left column) in such a way that eye movement in space (Fig. 3 right column) does not change. This tendency was confirmed by the left ear stimulation in prone position, as well as the right and left ear stimulation in supine position (Arai and Suzuki 1999)

One reason that we seldom recognize caloric second phase in patients as well as in normal subjects is that we have not considered this special orientation of the second phase. I carefully looked for the presence of roll nystagmus by infrared video monitoring during routine caloric testing but without success. It may be due to the small amplitude of roll nystagmus when looking in front of the eye, where

Fig. 2 Caloric second phase changed the direction by changing the position.

Eye position recordings of caloric nystagmus by right ear cold stimulation in prone. H; horizontal component, V; vertical component, T; roll component. The calibration bars indicate 40°. The strong and long lasting CCW nystagmus (T) as the second phase (upper column), that was repeatable (lower column), and changed direction to up after changing (shaded area) the position to right-side-down position.

Position	EYE in Head	EYE in Space
Prone		
Supine		
Upright		
R-ear down		
R-ear up		

Fig. 3 Simplified schema of the predominant quick direction of caloric second phase in different head positions.

Caloric nystagmus was induced by right-ear irrigation in prone. (from Arai et al 1999).

the rotational axis of the roll component is in tangential. In contrast, HOR and VER eye movement are looking at the equator, where eye displacement by the same angle of rotation is maximum. If we record roll component, we may find the second phase. If we stick recording by EOG, then recording with the subject in upright position instead of keeping in supine or prone position might permit the detection of the second phase.

With this idea, Kawachi examined caloric testing of 20 healthy volunteers in supine or prone position using EOG. When the caloric nystagmus was definitely completed (no nystagmus for more than 10 seconds), she changed the subject's position 90 degrees to upright. Then horizontal nystagmus appeared in the opposite direction to the first

phase in all tested subjects. The averaged velocity was 20% of the maximum velocity of the first phase in supine. The duration was nearly the same (120%) as the first phase (Kawachi 1992).

These spatial properties of caloric second phase remind us of cross-coupling of the velocity storage integrator (Raphan and Cohen 1988). They found that yaw OKAN elicited in right-side-down position (Fig. 4B) was much shorter and smaller than that in upright position (Fig. 4A). Instead, the OKAN had strong vertical component. When yaw OKN was elicited in supine position, the OKAN contained strong roll component. They call this phenomenon as "cross-coupling" of yaw OKAN to earth vertical axis, and considered as an important property of the velocity storage.

Instead of the spatial properties of caloric second phase, those of caloric first phase are needed clarification.

iii) orientation of caloric nystagmus

To extract the velocity storage component in caloric nystagmus, the orientation of caloric first phase has to be analyzed. From the three velocity traces of the caloric nystagmus, quick eye movements were eliminated. We are left with the slow phases, which were connected. Then, we have "caloric vector" which is defined by the three components of slow phase velocities of caloric nystagmus in a head fixed coordinate axis. The length of the caloric vector, which represents the amount of response, can be calculated. Each component of caloric nystagmus decayed

Fig. 4 "Cross-coupling" of yaw OKAN, (from ref Raphan and Cohen 1988).

Yaw OKAN in upright position (A) and in right ear-down position (B). In the upper traces, horizontal (H), vertical (V) and roll (R) eye position (POS) and the velocity (VEL), and photocell (P CEL).

Note that yaw OKAN (B: H VEL) in side position is much shorter and smaller than that in upright (A: H VEL). Instead, the OKAN had strong vertical component (B: VEL). Raphan and Cohen called this phenomena as "cross-coupling" and considered as an important property of the velocity storage.

Fig. 5 Head fixed 3D axis under right-hand-rule to express caloric vector.

to zero and reverse the direction to become the second phase, however, not always at the same time. That is, caloric vector does not always go through zero before building up to the second phase. Therefore, the end point of the caloric first phase must be defined as the time point showing minimum length after the peak response (Arai *et al* 1999).

In order to examine the orientation of caloric vector, the decaying part of the caloric first phase was windowed and plotted in 2D planes or a 3D cube. The three coordinate axes are defined by the three rotational axes by the right hand rule. That is, as for **yaw** component, leftward slow phase eye velocity (eyes move to the tip of four fingers of the gripped right hand) is expressed on a head vertical axis (**Z axis**) with the positive side directing to the top of the head (tip of the extended thumb) in positive. As for **pitch** component, downward velocity (four fingers of the gripped right hand) is expressed on an inter-aural axis (**Y axis**) with the positive side directing to the left ear (the extended thumb) in positive. As **roll** component, Clockwise slow phase eye velocity (four fingers of the gripped right hand) is expressed on a naso-occipital axis (**X axis**) with the positive side directing to the nose (the extended thumb) (Fig. 5).

A trajectory of 3D caloric vector in prone position is shown in a head-vertical and earth-vertical cube (Figs. 6D and H). In 2D presentations (Figs. 6A-C), plots of five normal animals are superimposed in red for the right ear, and in blue for the left ear stimulation. The maximum vector length is referred to as plus or minus one. The

trajectory are limited to two quadrates; the head-vertical positive to earth-vertical positive quadrant, and head-vertical negative around earth-vertical negative quadrant (Fig. 6A painted in yellow). In supine position, yaw and pitch components are reversed, but roll is not reversed. As a result, the trajectory is distributed in the same two quadrants as in the prone position; head-vertical positive to earth-vertical positive quadrant, and head-vertical negative to earth-vertical negative quadrant. According to Raphan and Cohen (1988), the central vestibular integrator, which they named "velocity storage", receives yaw eye velocity, store it with a time constant of about 15seconds, and releases in the earth vertical direction. Thus we may predict that the velocity storage component operates in the yaw positive (head-vertical positive) to earth-vertical positive quadrant and head-vertical negative to earth-

Fig. 6 Orientation of caloric vector in prone normal (A-D) and plugged (E-H) animals.

The trajectories of caloric nystagmus was normalized by the length of vector at the culmination as ± 1.0 . The falling phase of caloric first phase was windowed and plotted on yaw-roll (A,E), yaw-pitch (B,F) and pitch-roll (C,G) plane. In Prone position, roll and yaw components reversed after all-canal plugged (E-H). 3D drawings of the representative example are shown D and H. Responses from the left ear stimulation are in blue, those from the right ear stimulations are in red. The head positive-earth positive or head negative-earth negative quadrate are marked by light yellow.

vertical negative quadrant, coinciding with the caloric trajectory of normal animals.

We have two monkeys, which underwent surgically plugging of all 6 semicircular canals, and the success of plugging surgeries was confirmed histologically in one animal. The both monkeys equally lost reactivity to low frequency rotation (Yakushin 1989), but responded to calorization. In normal monkeys, the presence of convection current in the vertical canals, which surely change according to the head position, is not known. All-canal-plugged animals are useful to study mechanism of caloric nystagmus, because thermal activation of the labyrinth does not affect by head position. In the upright and supine positions, there was hardly any difference before and after the plugging. In prone (Figs. 6 E-H) and in side-down positions, the yaw component was changed in plugged animals compared to before plugging, i.e. plugging abolished the reversal of yaw component as a result of position reversal, indicating loss of convection in the lateral semicircular canal. In the head-vertical to earth-vertical plane, the trajectories fall in the same quadrants (in yellow) as before plugging, even though the right and left responses were inverted. These results indicate that plugging eliminates the convection current, and that the responses contain velocity storage activity.

Conclusion

Methods to elucidate the mechanism of caloric nystagmus were reviewed historically in three stages, 3D qualitative analysis by direct observation, 1D with quantitative analysis by EOG and 3D with quantitative analysis by search coil technique. Three dimension analysis of caloric nystagmus with and without all-semicircular-canal plugging clarified the contribution of convection current of the lateral canal, the non-convective component in the plugged canals which might be enhanced after plugging, and the velocity storage integrator.

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