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The Clinical Significance of the Caloric Second Phase Provoked by Positional Change in Vertiginous Patients

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Abstract: The reversal phase of caloric nystagmus is provoked when the lateral semicircular canal in a patient is reoriented from a vertical to a horizontal plane at the cessation of the caloric first phase, which we called the *provoked caloric second phase*. In investigating the clinical significance of the provoked caloric second phase, we recruited 102 vertiginous patients who had measurable caloric responses in both ears but no disorders of the central nervous system. We recorded the provoked caloric second phase in 188 (92%) of 204 ears in 102 patients. The average maximum slow-phase velocity of the caloric first phase was 26.9 degrees per second, and that of the provoked caloric second phase was 5.0 degrees per second. The maximum slow-phase velocity of the provoked caloric second phase correlated with that of the foregoing caloric first phase ($r = -.84$). Thus, we consider that the provoked caloric second phase is influenced largely by the foregoing caloric first phase. Furthermore, in the patients who responded normally to caloric stimulation, the directional preponderance of the provoked caloric second phase correlated with the directional preponderance of optokinetic after-nystagmus ($r = .64$). Hence, we conclude that the provoked caloric second phase reflects central vestibular asymmetry in patients with normal peripheral vestibular function.

Key Words: caloric nystagmus; human; optokinetic after-nystagmus; positional change; second phase

The caloric test was first introduced in neurootology by Barany in 1906 [1]. Since then, the caloric test has become one of the most important and widely applied vestibular tests to detect the peripheral vestibular dysfunction of each ear separately. The caloric second phase, however, rarely was discussed, as it occurs without positional change only in patients with severe neurological diseases, such as spinocerebellar degeneration.

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The reversal phase of caloric nystagmus is known to occur when the lateral semicircular canal is reoriented from the ampulla-up and vertical position to horizontal position after the cessation of a caloric first phase. However, the clinical significance of the phenomenon is controversial. Some authors consider the phenomenon pathological, whereas others regard it as physiological. Boeninghaus [2] observed the reversal phase of caloric nystagmus provoked by positional change in 9 ears of 20 normal patients. He explained that the phenomenon was a result of the reversed convection flow of the endolymph. He thought that in some patients the lateral semicircular canal coincidentally crossed over the horizontal plane, at which time it was reoriented. Kulmar et al. [3] observed the same phenomenon in 3 patients with posterior cranial fossa lesions (2 cases of Arnold-Chiari malformation and 1 with multiple sclerosis) but in none of this group's 11 normal patients.

Thus, they concluded that the phenomenon was a sign of a posterior cranial fossa lesion [3].

Conversely, Kawachi [4] recorded the phenomenon in all 36 ears of 18 normal patients. Murofushi et al. [5–7] also recorded the phenomenon in 37 ears of 22 normal patients. Both considered the phenomenon to be physiological.

In this study, we called this phenomenon the *provoked caloric second phase* and investigated its clinical significance in vertiginous patients.

PATIENTS AND METHODS

We obtained data from 102 vertiginous patients (30 male, 72 female) aged 13–79 years (mean, 48.6 years; standard deviation [SD], 16.8 years). These patients visited Tokyo Women's Medical University, Medical Center East, between January 2004 and April 2005 and fulfilled seven criteria: (1) no spontaneous nystagmus in total darkness with eyes open and with eyes closed; (2) no positioning nystagmus when examined by the Stenger maneuver [8] and by the Dix-Hallpike maneuver [9]; (3) no severe central nervous system disease (an acoustic tumor limited to within the internal auditory canal and judged as a peripheral lesion and small lacunar infarctions without focal signs in senile patients considered normal for age); (4) the caloric first phase provoked in both ears; (5) the visual suppression test [10], performed during the caloric test, normal in both directions; (6) optokinetic nystagmus provoked normally in both directions; and (7) electronystagmography (ENG) recordings in good condition.

The second phase was provoked as follows. With eyes open in a dark room, the patient lay supine on a bed, wearing covered goggles mounted with an infrared charge-coupled device camera. The head of the patient was tilted so that one ear faced the ceiling. Caloric stimulus was given by pouring 5 ml of tap water at 20°C into the upward-positioned ear for 15 seconds. At 20 seconds from the start of the irrigation, the head of the patient was brought back to a supine position with the neck anteflexed at 30 degrees. At the peak of the caloric first-phase response, the nystagmus was suppressed by taking off one of the covers of the goggles and letting the patient look at a penlight 30 cm away from the face (visual suppression test).

Ten seconds after the last beat of the caloric first phase, the patient's upper body was lifted upright with the neck anteflexed 30 degrees so as to place the lateral semicircular canal earth-horizontal to provoke the reversal phase. The entire maneuver was recorded by a binocular ENG through Ag/AgCl electrodes with simultaneous observations of eye movements using an infrared charge-coupled device camera. We excluded patients who were brought to the sitting position more than 20 seconds after the last beat of the first phase.

The intensity of both the caloric first phase and the provoked caloric second phase were evaluated using the maximum slow-phase velocity (SPV) of the nystagmus, which we measured manually. In this study, we referred to the maximum SPV of the right-beating nystagmus as a positive value and that of the left-beating nystagmus as a negative value unless stated otherwise.

We performed the optokinetic after-nystagmus test (OKAN) in accordance with the Sakata method [11]. We applied optokinetic stimuli of a constant acceleration by 1 degree per second squared for 80 seconds by projecting the random dots on the screen with a visual field of 160 degrees. When the speed reached 80 degrees per second, we kept this maximum speed constant for 10 seconds. Then all the lights were suddenly switched off. The eye movements were recorded by a binocular ENG with eyes open in darkness. We manually measured the duration of the OKAN.

We calculated the directional preponderance (DP) of the caloric first phase, the provoked caloric second phase, and the OKAN as $DP = |(a - b)/(a + b)|$. For the DP of the caloric first phase and for the provoked caloric second phase, a was the absolute value of the maximum SPV of the right-beating nystagmus, and b was that of the left-beating nystagmus. For the OKAN, a was the duration (in seconds) of the right-beating OKAN, and b was that of the left-beating OKAN. We presented DP in absolute value, so that the positive value of DP indicates that the right-beating nystagmus is stronger (or longer) than the left-beating nystagmus. We used the Student's t test to obtain the correlation coefficient. All data are presented as mean ± SD unless stated otherwise.

RESULTS

Provocation Rate and Intensity of the Provoked Caloric Second Phase

We recruited only those patients who showed caloric first phase in both ears, which resulted in a provocation rate of the first phase of 100% in 204 ears in 102 patients. We directed the caloric first phase opposite to the cold-irrigated ear in all patients with the average maximum SPV of 26.9 ± 14.1 degrees per second.

We provoked the caloric second phase in 188 ears (92%) of 204 ears in 102 subjects. Among those 188 ears, we provoked the second phase in both directions in 89 patients and in only one direction in 10 patients, and it was absent in both directions in the remaining 3 patients. The average maximum SPV of the provoked caloric second phase was 5.0 ± 3.8 degrees per second

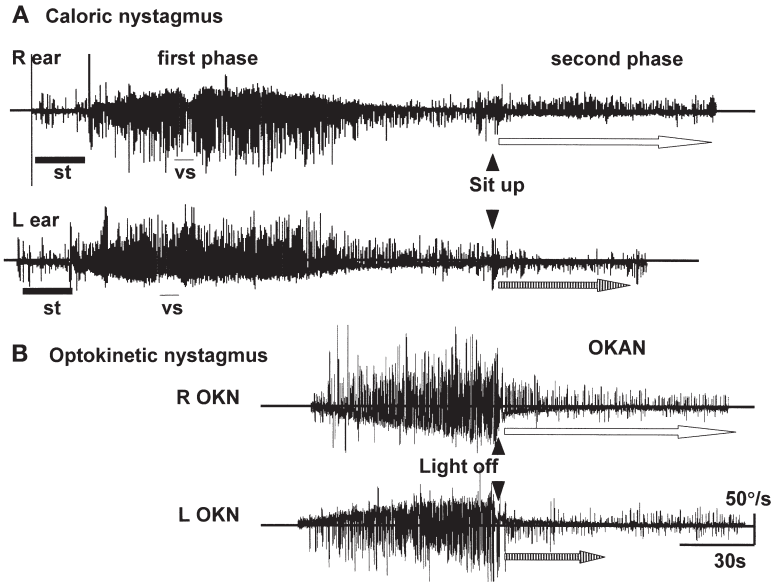

Figure 1. Electronystagmography recording of the horizontal eye velocity (time constant [tc] = .03) of a 65-year-old male patient. (A) The caloric first phase and the provoked caloric second phase (arrow). *st* = caloric stimulation with 5 ml water irrigation at 20°C; *vs* = visual suppression test. (B) Optokinetic nystagmus (*OKN*) and optokinetic after-nystagmus (*OKAN*; arrow). The upward deflection of the fast phase indicates right-beating nystagmus. Open arrows indicate right-beating nystagmus, whereas striped arrows indicate left-beating nystagmus. Distinct directional preponderance tendency to the right was recognized in the OKAN and also in the provoked caloric second phase.

in 102 patients, when we calculated the maximum SPV of the absent second phase as 0 degrees per second.

Among those 102 patients, the DP of the caloric first phase was <.15 in 38, which we defined as normal caloric response, whereas in other patients, the DP of the caloric first phase was ≥.15, which we defined as abnormal. In those 38 caloric-normal patients, the average maximum SPV of the first phase was 29.5 ± 13.3 degrees per second, and that of the provoked caloric second phase was 5.0 ± 2.9 degrees per second.

Figure 1 exhibits the ENG of the provoked caloric second phase recorded in a 65-year-old man. As in this recording, in most of the patients the first phase was vivid and appeared in a definite crescendo-decrescendo form, whereas the provoked caloric second phase was small and monotonous, showing no peak.

We compared the direction and intensity (maximum SPV) of the caloric first phase and those of the provoked second phase in 102 patients, the results of which revealed a strong correlation ($r = -.84$; Fig. 2).

Correlation with the OKAN

In 74 of 102 patients, we could calculate both DP of the provoked caloric second phase and DP of the OKAN. In those 74 patients, we compared the DP of the provoked caloric second phase and that of the OKAN and found no correlation ($r = .27$; Fig. 3A). Also, of those 74 patients, 38 had a caloric-normal response (DP of first phase <.15), and the others had an abnormal response (DP of first phase ≥.15). In those 38 patients who responded normally to caloric stimulation, correlation between the DP of the provoked caloric second phase and that of the OKAN increased ($r = .64$; see Fig. 3B).

An example of the ENG recording is shown in Figure 1. In this patient, caloric first phase and optokinetic nystagmus were almost equal in both directions. Nevertheless, distinct DP to the right was visible in the provoked caloric second phase and in the OKAN.

Correlation with the Caloric First Phase

We compared the DP of the provoked caloric second phase with that of the foregoing first phase. The afore-

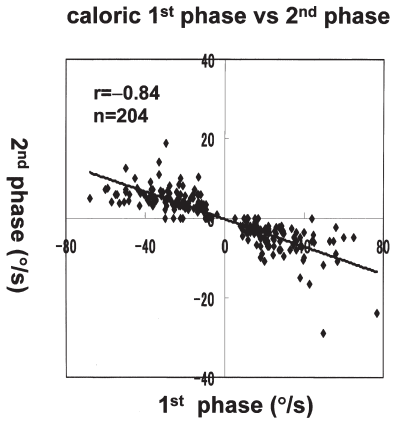

Figure 2. Correlation between the direction and intensity (maximum slow-phase velocity) of the provoked caloric second phase and the direction and intensity of the first phase of 204 ears in 102 patients. The maximum slow-phase velocity of the right- or left-beating nystagmus was referred as a positive or negative value, respectively.

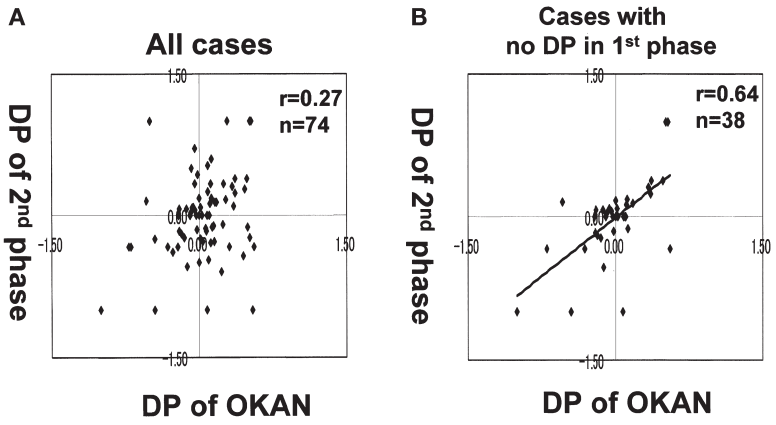

Figure 3. Correlation between the directional preponderance (*DP*) of the provoked caloric second phase and the DP of the optokinetic after-nystagmus (*OKAN*). (A) Correlation in 74 patients in which both DP of the provoked caloric second phase and that of the OKAN could be measured. (B) Correlation in 38 patients (of the aforementioned 74) in which DP of the first phase was <.15.

mentioned 74 patients—in which both the DP of the second phase and that of the OKAN could be measured—were recruited in the study. In those same 74 patients, the DP of the first phase and that of the provoked caloric second phase were weakly correlated ($r = -.37$), as shown in Figure 4A. Of those 74 patients, 37 demonstrated that the DP of the OKAN was <.15, which we regarded as no DP in the OKAN; in the others, the DP of the OKAN was ≥.15. When we limited the patients to the 37 with no DP in the OKAN, the correlation increased ($r = -.48$; see Fig. 4B).

DISCUSSION

Intensity of the Provoked Caloric Second Phase

Kawachi [4], who used the same provocation method as did we, reported the average maximum SPV of the caloric first phase to be 28.5 degrees per second and that of the provoked caloric second phase to be 5.4 degrees per second in 18 normal patients. Our results, especially those from the caloric-normal group (38 of 102 patients), showed similar responses.

Murofushi [5], who also provoked caloric second phase by positional change, reported the average maximum SPV of the caloric first phase to be 29.8 degrees per second and that of the provoked caloric second phase to be 1.5 degrees per second in 22 normal patients. The intensity of the first phase was almost the same as ours, though that of the second phase was definitely smaller. Two reasons can be considered: Murofushi's subjects wore Frenzel glasses, which blocked the patients' vision incompletely and suppressed the second phase. Additionally, if Murofushi's patients were repositioned later than under our timing (10–20 seconds after the last beat of the first phase), the second phase might be suppressed.

In our study, the direction and the maximum SPV of the provoked caloric second phase correlated strongly with those of the first phase ($r = -.84$; see Fig. 2). We assume that the energy to produce the caloric second phase accumulates during the first phase according to the strength of the first phase. Although this energy may be influenced from the central vestibular system, we consider that it is the caloric first phase that mainly determines the direction and the strength of the second phase.

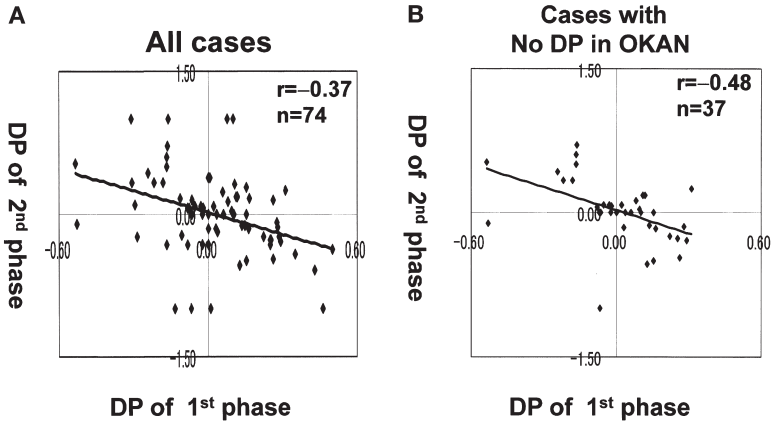

Figure 4. Correlation between the directional preponderance (*DP*) of the caloric first phase and that of the provoked caloric second phase. (A) Correlation in 74 patients in which both DP of the provoked caloric second phase and DP of the optokinetic after-nystagmus (*OKAN*) could be measured. (B) Correlation in 37 patients (of the aforementioned 74) in which DP of the OKAN was <.15.

Correlation with the OKAN

In 74 of the 102 patients, the DP of the caloric second phase and that of the OKAN could be definitely measured. These 74 patients included 38 caloric-normal patients (absolute value of first-phase DP, $<.15$) and 36 caloric-abnormal patients (absolute value of first-phase DP, $\geq.15$). We compared the DP of the provoked caloric second phase with that of the OKAN. Among those 74 patients, we found no correlation ($r = .27$; see Fig. 3A). However, in the 38 patients with normal caloric response, we found a correlation ($r = .64$; see Fig. 3B). The OKAN is considered to be a direct reflection of a velocity storage integrator in the brainstem [12–15]. The DP of the OKAN in vertiginous patients with normal peripheral vestibular function indicates the asymmetry of the velocity storage integrator. Therefore, we believe that the DP of the provoked caloric second phase reflects central vestibular asymmetry in those patients with normal vestibular function.

Correlation with the Caloric First Phase

The DP of the caloric first phase correlated weakly with that of the provoked caloric second phase ($r = -.37$; see Fig. 4A). When we limited the patients to those with no DP in the OKAN, this correlation increased ($r = -.48$; see Fig. 4B). The DP in the OKAN reflected central vestibular asymmetry. The less the asymmetry in the central vestibular system, the more clearly would the provoked second phase reflect the peripheral vestibular function.

Origin of the Provoked Caloric Second Phase

Arai et al. [16–18] analyzed the caloric second phase of monkeys (which occurs very strongly without positional change) three-dimensionally using magnetic search coils. The caloric second phase appeared predominantly as torsional nystagmus in the supine and prone positions. Additionally, it appeared as vertical nystagmus in the side position, and it appeared as horizontal nystagmus in the upright position. Therefore, these authors concluded that the caloric second phase tended to beat most strongly on the earth-horizontal plane in monkeys.

Kawachi [4] considered that the caloric second phase also appears on the earth-horizontal plane in humans as in monkeys, which Kawachi explained as follows: In humans as in monkeys, the caloric second phase appears as torsional nystagmus in the supine position. As normal ENG does not detect torsional nystagmus, the second phase cannot be recorded as long as the patient remains in the supine position. However, when the patient is reoriented to the upright position, the torsional nystagmus changes to horizontal nystagmus and could be registered as the provoked caloric second phase.

Conversely, Murofushi et al. [5–7] elucidated the provoked caloric second phase to be mainly a vestibular adaptation. They explained as follows: The duration of the caloric first phase is generally near 180 seconds [19], which is much shorter than the thermal recovery of 10 minutes [20]. At the time when the caloric first phase finishes, cupular deflection by convection still exists, but the nystagmus is cancelled by adaptation. When a patient's lateral semicircular canal is brought to the earth-horizontal plane, the convection stops, and the adaptive nystagmus becomes apparent.

We believe that both mechanisms participate in the origin of the provoked caloric second phase. The vertical and horizontal nystagmus are reported to have appeared at the same time when supine patients were reoriented to the side position after the cessation of the caloric first phase [4]. If the caloric second phase beats on the earth-horizontal plane, it should appear as vertical nystagmus in the side position. If the caloric second phase is generated by the released adaptation mechanism, it should appear as horizontal nystagmus in the side position.

In our study, 16 ears did not show the provoked caloric second phase. The maximum SPV of the first phase of the 16 ears was 16.2 ± 10.3 degrees per second. It was much smaller than the average maximum SPV of all 102 patients (26.9 degrees per second). We presume that when the first phase is very weak, the energy does not accumulate sufficiently to produce the detectable second phase. Additionally, both lack of alertness and incomplete blocking of vision (e.g., dim light from the computer screen) might suppress the provocation of the caloric second phase.

Does the Provoked Caloric Second Phase Detect the Central Imbalance?

Many patients with normal caloric responses still complain of dizziness. The directional asymmetry of the central velocity integrator is one of the reasons for the dizziness of these patients. From our study, we think the provoked caloric second phase reflects central vestibular imbalance in patients with normal peripheral vestibular function. This provocation of the caloric second phase by a positional change can be performed easily without any special equipment in daily practice. Therefore, we consider that the provocation of a caloric second phase is a useful method to detect central vestibular asymmetry in vertiginous patients who display a normal caloric response, assuming sufficient attention is paid to the appropriate timing of the positional change and to the sufficient blocking of affected patients' vision.

CONCLUSION

The reversal phase of caloric nystagmus was provoked by positional change, which we called the *provoked caloric second phase*. This provoked caloric second phase was recorded in 188 ears (92%) of 204 ears in 102 vertiginous patients. The direction and the maximum SPV of the provoked caloric second phase correlated strongly with that of the foregoing caloric first phase ($r = -.84$). Thus, we conclude that the second phase is determined mainly by the foregoing first phase. Among the patients who responded normally to caloric stimulation, the DP of the provoked caloric second phase correlated with that of the OKAN ($r = .64$). Therefore, we think the provoked caloric second phase reflects the central vestibular asymmetry in patients with normal peripheral vestibular function.

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