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*«**ΑΚΟΟΛΟΓΙΑ & ΝΕΥΡΟΩΤΟΛΟΓΙΑ**»*

Διπλωματική Εργασία

«Electronystagmography caloric test – its use in clinical practice (a systematic review)»

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του Δημητρίου Τσαρπαλή

με Θέμα: «Electronystagmography caloric test – its use in clinical practice (a systematic review)»

Ακαδημαϊκό Έτος 2018-2019

ΑΘΗΝΑ ΝΟΕΜΒΡΙΟΣ 2019

Με αγάπη στο γιο μου Ιάσωνα

Θα ήθελα να εκφράσω τις ευχαριστίες μου στους κύριους καθηγητές Θωμά Νικολόπουλο και Αθανάσιο Μπίμπα, καθώς και σε όλους τους συντελεστές του μεταπτυχιακού προγράμματος γιατί μου έδωσαν την ευκαιρία να εμβαθύνω στο αντικείμενο της ακοολογίας-νευροωτολογίας. Επίσης θα ήθελα να ευχαριστήσω τους γονείς μου, Κυριάκο και Αναστασία, για τη στήριξη που μου παρείχαν όλο αυτό το χρονικό διάστημα.

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I. Abstract

Electronystagmography caloric test has stood the test of time and has been proven to be clinically invaluable when dealing with dizzy or vertigo patients. It is an objective test to diagnose vestibular disorders (peripheral and central). (1, 2) Since Fitzgerald and Hallpike first described the alternate binaural bithermal caloric test (ABBT) in 1942, the ice water caloric test (IWCT), the monothermal caloric screening test (MCST), the simultaneous binaural bithermal caloric test (SBBT) and the monothermal differential caloric test (MDCT) have been developed. (3, 4) Even nowadays, the alternate binaural bithermal caloric test (ABBT) remains the standard caloric test used because each horizontal semicircular canal is serially examined, its caloric response is reproducible and overall the test is well tolerated. (3, 4, 5) However, we should keep in mind that certain studies have shown that this laboratory test in up to 25% of patients failed to aid physicians to draw any conclusions as the caloric test is a low frequency sinusoidal harmonic acceleration test of around 0.004 Hz, assessing partially the function of each horizontal semicircular canal. (1, 2, 3) Normal ENG caloric test results do not necessarily imply a normal vestibular function. A no response to caloric stimulus does not mean a non-functioning peripheral vestibular organ, as its middle and high-frequency function have not been examined as well as the other two semicircular canals. Many ENG caloric abnormalities are non-localizing; therefore, clinical history and otologic examination as well as other laboratory methods are needed to formulate a diagnosis and treatment plan. (6) In terms of cost-effectiveness for evaluating vertigo, it has been shown that hearing testing followed by electronystagmography and especially caloric testing is the most effective method. (7) ENG caloric test findings are more accurate than clinical symptoms in predicting whether imaging tests will be abnormal. (7)

II. Introduction

Electronystagmography is the gold standard among laboratory methods evaluating the vestibular system. Based on its results, the decision to proceed with more expensive tests like MRI is made. (7) It consists of a battery of tests, collectively named ENG testing. It is named after the DC potential that naturally exists between the cornea and the retina (the corneo-retinal potential) used to track eye movements in electrooculography. It evaluates the vestibular system by testing the vestibulo-ocular reflex (VOR). Duration, frequency (beats/time period), mean peak slow-phase-eye velocity of nystagmus (spv) (degrees/second) as well as unilateral weakness (UW) and directional preponderance (DP) are being measured or calculated. (8)

Electrooculography (i.e. skin surface electrodes recording corneo-retinal potential changes), till recently, was the most popular method of monitoring eye movements when assessing the VOR. Nowadays, videooculography is widely used. An infrared goggle apparatus employing the photoelectric effect of differential reflection between the iris and the sclera is preferred over electrooculography. (4, 8, 9) In the beginning of the development of electronystagmography, eye movements were recorded on graph paper using polygraph recorders. In the 80's, video recording became available as well as computer systems. Nowadays, computers' software provides sophistication of analysis, calculation, retrieval and storage of caloric test and its results, making manual measurements or calculations almost obsolete. (8, 9)

The ENG test battery consists of three groups of tests. (9, 10)

The first group of tests detects the presence of abnormal eye motility and whether it changes with different head positions (positioning and positional tests). (9, 10) The gaze test evaluates gaze stability, eye movement limitations, ocular flutter, spontaneous and latent nystagmus. (9) The Dix-Hallpike maneuver evaluates for benign paroxysmal positional vertigo (BPPV). (9) The positional test investigates the presence of nystagmus as head assumes different positions. (9, 10)

The second group examines the visual-oculomotor function. (9, 10) The saccade test detects disorders of the saccade movement control system by analyzing latency, accuracy and velocity of eye motility from one given point to another one. (9, 10) The smooth pursuit test assesses eyes ability to track a smoothly moving target. (9, 10) The optokinetic test evaluates the optokinetic reflex as eyes follow moving objects, e.g. an optokinetic drum while the head is still. (10) The smooth pursuit and the optokinetic test detect any anomalies of the pursuit system. (9, 10)

The third group, the caloric tests evaluate vestibulo-oculomotor function. The caloric test detects dysfunction of the labyrinth (horizontal semicircular canal) or vestibular nerve (superior division). (6) The alternate binaural bithermal caloric test (ABBT) is the standard caloric test examining each vestibular organ individually. Caloric testing should be conducted last, after the first and second groups of tests have been undertaken. (4)

III. The Vestibulo-Ocular Reflex (VOR)

The vestibulo-ocular reflex (VOR) is an involuntary reflex with afferent input from the labyrinth whose purpose is to stabilize images on the retinas during head movement by producing eye movements in the direction opposite to head movement, thus preserving the image on the center of the visual field. (11) For example, when the head moves to the right, the eyes move to the left and vice versa in order to maintain the image on the fovea. (11, 12) Since slight head movement is present all the time, the VOR is necessary for stabilizing vision. (11) It has been shown that eye movements lag the head movements by less than 10ms, thus making the VOR one of the fastest reflexes in the body. (11) Signals from the labyrinth are sent as directly as possible to the eye muscles as their connection involves only three neurons, collectively called the three neuron arc. (11)

The VOR has both rotational and translational aspects, depending on whether the head performs a rotational or a translational movement. (11, 12) The former elicits the rotational or angular VOR, that is, when the head rotates to the right, the RVOR causes the eyes to rotate to the left, so that the gaze remains stable. The latter triggers the translational VOR, that is, when the head translates to the left, the TVOR rotates the eyes to the right to compensate for the relative motion of near targets on the retina. (12) Natural head movement comprises both rotation and translation. (12)

The VOR is not dependent on visual stimuli. It can be elicited by caloric (hot or cold) stimulation of the inner ear (caloric test) or by head thrust (head impulse test). It works in total darkness or when the eyes are closed. However, in the presence of light, the fixation reflex is added to the movement. (11) In the unconscious patient, the VOR can be driven through the use of caloric test or doll’s eye test. (12) It can be used in the comatose patient to demonstrate that the brainstem still functions normally, as the depressed cortex does not override the reflex. (12)

The gain of the VOR is defined as the change in the eye angle divided by the change in the head angle during the head turn. Ideally, the gain of the rotational VOR is 1.0. The gain of the vertical and horizontal VOR is usually close to 1.0, but the gain of the torsional VOR (rotation around the line of sight) is generally low. If the gain of the VOR is not close to 1, the head turn results in image motion on the retina. Motor learning is initiated to make the necessary adjustments to the gain, thus giving rise to VOR adaptation. (11) Recent research has indicated that there are mechanisms to suppress VOR, for example in the case of head-free pursuit of moving targets, where VOR is counterproductive to the goal of reducing retinal offset, active visual feedback is used. (11) It has been shown that extra-retinal signals are recruited to aid pursuit movements by VOR suppression when there is no visual feedback. (11)

VOR displays a remarkable capability of adaptation, modifying its dynamics so as to secure visual stability under any circumstances, in which mismatched head movement and visual input impair visual stability. It has been shown that the site of this adaptation resides in the flocculus, evolutionarily the oldest area of the cerebellum. (12)

The three semicircular canals of each inner ear are responsible to sense angular acceleration within any plane and connect directly with the ocular motor nuclei. The otolith receptors, utricle and sacculus, are activated respectively for horizontal (utricle activation) and vertical (sacculus activation) translational movements. They are involved in a tilt reaction stimulated by gravity. (12, 13) The neural integrator for horizontal motion is located in the nucleus prepositus hypoglossi in the medulla, whereas the neural integrator for vertical and torsional movement was found to be in the interstitial nucleus of Cajal of the rostral midbrain and vestibular nucleus. (11, 12) The same neural integrators process signal coding for saccades, smooth pursuit and optokinetic movements. (11, 12) Signals are transmitted via the vestibular nerve through the vestibular ganglion and end in the vestibular nucleus, from which information is processed via several pathways. (11, 12) For horizontal movements, the areas of the abducens nucleus and medial longitudinal fasciculus (MLF) are activated. Lateral to the MLF, first and second order neurons with the aid of additional ascending tracts transmit vertical and torsional movement signals via brachium conjuctivum and MLF to the nuclei of oculomotor and trochlear nerves (cranial nerves III and IV). (12) Target position is maintained through the use of three signals: a) an initial movement signal, b) a tonic contraction signal and c) an eye velocity position signal. (12)

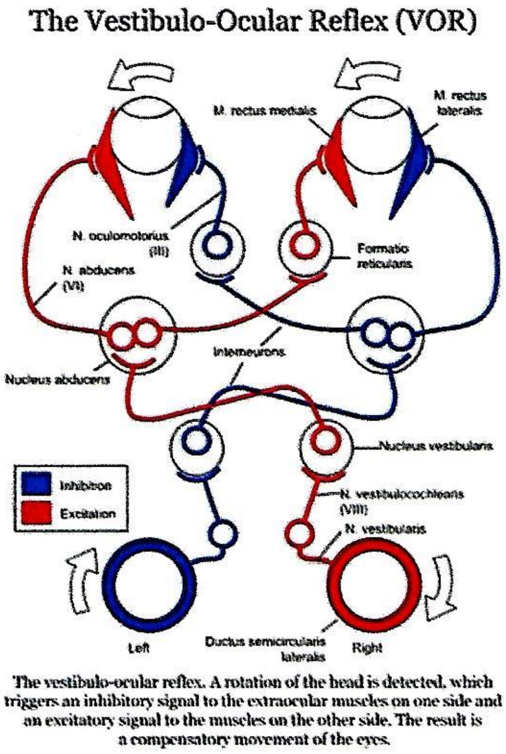

Figure 1: The main pathway for horizontal VOR. (Reproduced from Wikipedia) (11)

Another pathway (not in figure) projecting from the vestibular nucleus connecting the ascending tract of Dieters to the ipsilateral medial rectus motor neuron also exists. There is no direct neural circuit connecting vestibular neuron to medial rectus motor neuron. There are pathways exercising an inhibitory action to the ipsilateral abducens nucleus. (11)

IV. Caloric Test

The caloric test is the most important test in the ENG test battery, emphasizing the low frequency function of each horizontal semicircular canal separately, but still it is the most difficult and the most time consuming test of all. (3) Schmiederkam in 1868 first observed that water irrigation of the external auditory canals elicited nystagmus. (14) It was not until 1906 that Robert Barany postulated caloric convection theory. Electrooculography was first used to provide permanent records of nystagmus by Mittermaer and Jung. Henriksson and Stahle were the first to observe that nystagmus elicited by caloric testing is inhibited by visual fixation, thus doubting the previous common practice of performing the test with the examinees' eyes open, fixating on a stationary point opposite to them. (14)

Robert Barany in 1906 (Nobel Prize laureate in 1914 for his work on the vestibular system physiology) described that caloric irrigation causes changes in the endolymph density on the lateral aspect of the horizontal semicircular canal (that is closest to temperature source), thus creating a temperature gradient and respectively inducing endolymphatic flow in the affected canal of the stimulated ear. Gravity causes the endolymphatic fluid to move, deflecting the cupula. Nystagmus is observed as cupula deflections result in changes of the neural firing rate of the affected lateral labyrinth, thereby stimulating or inhibiting the vestibular nerve and its afferent pathway. (3, 5, 15) Barany's explanation was that caloric irrigation stimulation is analogous to a slow head rotation, thus initiating the VOR. Barany's theory can not explain the fact that even "dead ears" can elicit a caloric response, neither that the duration of caloric test is greater in the face-up than in the face-down position and that even caloric nystagmus can be induced even in zero gravity (microgravity of outer space). Also, in monkeys whose horizontal semicircular canals were occluded, a weak caloric response was observed. Up to date, no exact mechanism resolves the aforementioned issues. (3, 15) To sum up, current incomplete caloric response mechanism involves both the endolymphatic convection and the secondary direct effect of temperature change on the rate of discharge of the superior vestibular nerve. (15) Hot temperature causes an elevation of neural firing rate, whereas cold temperature causes the opposite. (15) Volume expansion of the endolymph due to thermal stimulation causes mechanical transduction as well. (14)

Various caloric stimuli (water or air) at different temperatures (hot, cold, bithermal, monothermal) with varying duration (5 to 60 seconds) on the external auditory canal (bilaterally and consecutively or simultaneously) have been tried by researchers. (5) Since Fitzgerald and Hallpike first described the alternate binaural bithermal caloric test (ABBT) in 1942, the ice water caloric test (IWCT), the monothermal caloric screening test (MCST), the simultaneous binaural bithermal caloric test (SBBT) and the monothermal differential caloric test (MDCT) have been developed. (3, 4) Even nowadays, the alternate binaural bithermal caloric test (ABBT) remains the standard caloric test used because a) each horizontal semicircular canal is serially examined, thus investigating partially each peripheral vestibular organ at a time, b) the caloric response is reproducible for almost all patients and c) the test is well tolerated by most of them, well-suited even for bedside evaluation of patients with cervical motion restrictions. (3, 4, 5)

Caloric test performance limitations/compromises

1) Caloric response is predominantly from the horizontal semicircular canal, since there is little impact of the temperature gradient on the vertical semicircular canals due to the anatomical arrangement and distance from the external auditory canal (Aw et al., 1998), (3)

2) Caloric testing stimulates the lateral semicircular canal at the low frequency range. Hamid et al. in 1987 by modeling the temporal course of the thermal stimulation as an equivalent sinusoidal wave, estimated that its effective frequency is about 0.004 Hz, meaning that a rotational stimulus of 0.004 Hz is needed in order a slow phase velocity nystagmus to be produced. However, these estimates can vary from 0.003 Hz up to 0.008 Hz should individual variations that exist among thermal stimuli are taken into consideration. Since caloric testing is a low frequency test of the horizontal semicircular canal, a no response to a hot, cold or ice stimulus, does not imply a non-functioning peripheral vestibular organ, as middle and high-frequency functions have not been examined. (3)

3) Strength of the caloric response depends on mental concentration and on visual fixation denial degree shown at the test. A low mental alertness will not discourage the examinee from suppressing the caloric induced nystagmus, thus a poor response will be accounted for. Examinees are given mental tasks to perform either at the beginning or after caloric irrigation, such as, to count backwards, to do multiplication or to name lists. (4, 5) Visual fixation is denied using any of the following ways: a) eyes open, wearing Frenzel goggles, b) eyes open in a dark environment, or c) eyes closed. Eyes open, fixating in an examination room with ample light was performed in the early era of caloric testing, but later on, with the advent of electrooculography (EOG), this was abolished. (5) Eyes closed lead to Bell's phenomenon (a slight upward and midline eye deviation), interfering with nystagmus (partially inhibiting it), thus it is not recommended. (16) In fact, Hood and Korres in 1979 have managed to totally cancel nystagmus by Bell's phenomenon. (17) When the eyes are open and fixating, the smooth pursuit system is activated, interacting with the VOR, thus affecting its response. (1) The least variation of caloric response has been shown in subjects with eyes open, denied fixation using Frenzel goggles or in total darkness, making these the preferable methods. (5) The British Society of Audiology (BSA, 2010) acknowledges that the optimal condition for recording caloric induced nystagmus is achieved when the patient has eyes open in darkness, gazing straight ahead. (Baloh et al.) Creating total darkness in an examination room can be difficult, so constant dim lighting is suggested to minimize corneo-retinal potential changes affecting electronystagmography, but not videonystagmography. (4)

4) Significant variations in the caloric response among patients and between ears even of the same patient have been observed, even though water or air irrigation parameters are controlled as well as possible because temperature gradient is very much dependent on bone structures and air in the middle ear cavity. (3, 14) This issue has been merely solved by comparing the responses from the right and the left horizontal canal at a given irrigation and not taking into consideration the absolute values of each ear (Jongkee's formula, 1962). Till now, an alternative formula besides that of Jongkee's has not been adopted, even though Jongkee's formula is characterized by its non-linearity and its underestimation of performance of peripheral vestibular organ for afferent nerve fibers or hair cells loss. (3) A curve-fitting approach (mathematical modeling) to the caloric response measuring VOR time constants was described by Formby et al in 2000 dealing with caloric test non-linearity. (18)

5) Furthermore, the assumptions of normal distribution and unequal variance of absolute values of slow phase velocity (spv) work well for the majority of cases, when slow phase velocity absolute values are within the range of 15 up to 40 degrees per second. The criterion of 20 to 30% difference of response between the right and the left lateral semicircular canal is easily achieved when spv is lower than 15 degrees per second, whereas for spv larger than 40 degrees per second, the same response difference would be obtained with much larger values. To sum up, large percentage difference of responsiveness between the left and the right ear with small absolute values and vice versa, small percentage difference with large absolute values may be erroneously reported. (3) The British Association of Audiology (BSA, 2010) states that the absolute values of unilateral weakness (UW) and directional preponderance (DP) will approximate the systematic errors if mean peak slow phase velocity (spv) for all four irrigations in the alternate binaural bithermal caloric test (ABBT) is less or equal to 5 degrees per second, thus rendering them (UW, DP) unreliable. (4)

Contraindications (strong and secondary)

Special precautions should be undertaken as certain health history situations (problems) may render a patient unfit to undergo the test. These include: 1) high blood pressure (acute or uncontrolled), 2) heart problems (unstable angina, cardiac arrhythmias, myocardial infarction the last 6 months), 3) seizures (acute, uncontrolled, status epilepticus), 4) psychotic disorder (acute, not controlled), 5) ear surgery (the last 6 months) and finally 6) eye surgery (the last 3 months). The above are strong contraindications. (4) Recently Kasbekar et al. (2010) failed to find any significant increase of mean blood pressure or heart rate associated with caloric test undertaken. Further studies of the effect of caloric testing on patients with well controlled cardiovascular diseases are deemed necessary. (4) Till then, the aforementioned precautions hold true.

Secondary contraindications present at the time of caloric test are: 1) external otitis, 2) middle ear effusion, 3) atrophic or hypermobile tympanic membrane and 4) wax. (4) Most physicians regard a middle ear compliance on tympanometry greater than 1.8 ml as unsafe for water irrigation. (4)

Pretest preparation (drugs and travel arrangement)

Patients who have been prescribed medications that may influence the result of the caloric test are strongly advised to discontinue their use for at least 48 hours prior to the test [British Society of Audiology (2010), American National Standards Institute (1999) as well as British Standards Association (1999) recommendations]. (3, 4) Drugs interfering with the vestibulo-ocular reflex (VOR), ocular motility or mental alertness may cause erroneously findings. (14) Vestibular sedatives/suppressants, anti-emetics, anxiolytics and antidepressants are the most common prescribed medications, having the potential to affect the test. (3, 14) Patients are also recommended to have a 48 hour period free of alcohol consumption (Jacobson et al., 1993). (4, 14) Anti-seizure drugs as well as antipsychotic ones have been exempted and no discontinuation prior to testing is advised. (3, 14) Clinical doctors should be aware of any drug interference to the test and interpret its findings accordingly, or even schedule another examination date if patient's medication compliance is incomplete. (14) Unfortunately, there are no dose related studies on quantitative findings of caloric testing. (3)

As certain patients will experience nausea and vomiting after caloric irrigations, it is recommended that patients do not eat for at least two hours before the test, are accompanied if possible and not allowed to drive or travel by themselves for no less than one hour. (4) Also, it is recommended patients not to wear any make-up, face creams or lotions because of possible interference with electrooculography or videooculography. (4)

Mental alerting tasks

The most effective mental alerting tasks are those that make patient use recall memory i.e. "name a country that begins with the letter ….", "name a color that begins with ....", "name a city in the state of ….". The less effective are questions like "what is your favorite food?", "what is your age?" or telling the patient to count backwards i.e. by 3's or 7's. (19) Interacoustics, the world leader in producing videonystagmography (VNG) equipment in its guides recommends that recall memory tasks be used to discourage the patient from impeding caloric nystagmus. (20) British Society of Audiology (BSA, 2010) recommends that a constant level of mental arousal should be maintained throughout the caloric nystagmus recording and any mental task adjustments deemed necessary should be advocated. (4) In cases of hearing impaired patients, clinical doctors should have informed them beforehand of the repetitive mental tasks they will be asked to perform and have established a code of communication i.e. "when I tap you on your shoulder, start naming countries beginning with the letter …." etc. (3, 14)

General Considerations

a) Patient's age

There is good correlation between aging and decreased vestibular response, regardless of measurement parameters quantifying caloric response (Mulch et al., 1979). (21) Most researchers have reported that patients aged 65 years or older show a decline in caloric response (Mulch et al., Bruner et al., Karlsen et al.) (21, 22, 23) Certain researchers have doubted the practical value of performing caloric test in the elderly associated with their health status. (Hajioff et al.) The American Speech-Language-Hearing Association (ASHA, 2008) claims that although there is no upper patient's age limit concerning caloric testing undertaken, there is a lower limit of 6 years old for children (developmental age including mentally retarded adults).

b) Optimal head position

Coats et al. in1967 studied the magnitude of caloric response of 12 subjects when their body position changed up to 360º. They found that the optimal head position for most intense caloric response was between 0 to 60º above the horizontal plane, ideally 30º above the supine position. (24) Blanks et al. in 1975 reported that the optimum angle of head position to the horizontal plane is determined by the vertical alignment of external ear canal and lateral canthus. (4) British Society of Audiology (BSA, 2010) plainly states that the best caloric test position is achieved when horizontal semicircular canal is lodged vertically. (4)

c) Time elapse between two consecutive caloric irrigations.

Most researchers suggest a time interval between irrigations of 5 minutes. American National Standards Institute (ANSI, 1999) suggests a minimum of 5 minutes. (10) British Society of Audiology (BSA, 2010) recommends a minimum of 7 minutes. BSA states that there is evidence that this interval can be as minimal as 3 minutes, however most recent research suggests a time elapse of 7 minutes. (14)

Brookler (1971, 1975) in his research concerning simultaneous binaural bithermal caloric test (SBBT) used a 5 minute interval between caloric stimuli. (25, 26) In Furman et al. study (1988) when comparing alternate to simultaneous bithermal caloric tests, warm caloric irrigations followed cold irrigations after a 5 minute interval . (27) Lightfoot et al. study (2009) of optimum criteria for monothermal caloric screening test (MCST) used a 7 minute interval from the start of one irrigation to the start of the next one. (28)

Shepard et al. (2016) taking a more practical stand, suggested that if no residual nystagmus is observed between irrigations, then clinical doctors may proceed to the next irrigation with a certain degree of safety. (3)

d) Caloric test duration

The alternate binaural bithermal caloric test (ABBT) will take approximately 25 minutes (20-30 minutes). As the monothermal caloric screening test (MCST) is a much shorter test, it will take around 14 minutes (10-14 minutes). Clinical doctors should add another 10 to 15 minutes to the ABBT duration, in case simultaneous binaural bithermal caloric test (SBBT) is undertaken. When assessing any low-frequency residual function of the peripheral vestibular organ, the completion of ice water caloric test (ICWT) will take no longer than 10 to 14 minutes.

e) Vestibular habituation

Multiple irrigations with the same caloric stimulation on the same ear result in decreased caloric response, thus vestibular habituation takes place. Fluur and Mendel showed that repeated warm water irrigations decreased the duration of caloric response, whereas, multiple cold water irrigations could make caloric nystagmus disappear. (29)

Special Considerations

Tympanic membrane perforation and/or middle ear surgery

Air or closed-loop water caloric irrigations are recommended in cases of tympanic membrane perforation and /or middle ear surgery. Open-loop water caloric irrigation is contraindicated. (2, 4, 14) Tympanic membrane perforation and/or middle ear surgery in one or both ears will result in an unequal heat transmission between the two ears. (2, 4, 14) Unilateral weakness (UW) and directional preponderance (DP) equations do not apply in these situations and caloric testing is solely performed to show any peripheral vestibular function at all. (2, 4, 14)

Barber et al. in 1978 observed that warm irrigation of ears with tympanic perforation elicited an initially opposite directed nystagmus, but soon after, nystagmus was beating as expected. This observation was attributed to mastoid bone moisture. At first, the warm caloric irrigation evaporates the moisture, thus cooling the middle ear cavity, but very soon the ear shows its expected behavior. (2, 3)

In cases of mastoidectomy with an intact ear drum, a shortened latency with a greater magnitude of caloric response will be measured. Shepard et al. recommend an initial 5 second caloric irrigation on the operated ear. If caloric response does not show any enhancement (short latency, large magnitude) due to surgery, then the clinical doctor may proceed to the complete irrigation. (3)

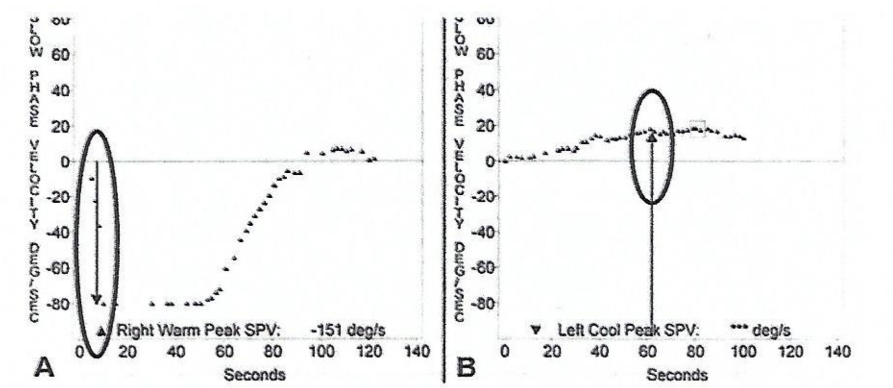

Figure A. SPV of right ear (canal wall down mastoidectomy). Within 5 seconds peak SPV has been reached. Figure B. SPV of left ear (not operated). (Reproduced from Shepard.) (3)

Water / Air caloric irrigation

Since the advent of caloric test, water has been the medium of choice for caloric irrigation. Water has a better performance over air because it provides a well-sustainable temperature difference, thus transferring more thermal energy than air does. (3, 28) Distilled water is recommended because tap water may contain debris or algae. (3, 14) Recently, humidified air has been tried to deliver a more effective thermal stimulus than dry air. (3)

There are two types of water irrigators: open- and closed-loop systems. (3, 14) In open-loop systems water is infused in the external auditory tube and recovered in a basin placed next to patient's ear. (3, 14) Modern open-loop water irrigators circulate water through the delivery tube at a specified temperature continuously, so no purging is necessary before commencing irrigation as before. (14) Closed-loop systems deliver water stimulus through an expendable balloon placed in the ear canal. Water flows continuously in the system and when in use travels from the delivery tube to the balloon and then back to the water bath and so forth. (14) In this way, purging and recovery are not an issue anymore. (14) Currently, there are no closed-loop irrigation systems in the market. (3)

Measurement parameters of caloric nystagmus

a) Duration

Nystagmus duration does not correlate to caloric response of horizontal semicircular canal. It is shown that it is directly proportional to the time endolymph takes to reach its original temperature. (14)

b) Latency

Nystagmus latency is the time frame between initialization of caloric irrigation and first observed nystagmus beat. It has a multifactorial dependence (e.g. endolymph convection and volume expansion, superior vestibular nerve firing rate, mental alertness etc.) (14, 15)

c) Amplitude

Amplitude refers to the eye movement during the slow phase of a nystagmus beat. On polygraph paper, it is measured from the base to the tip (in degrees). This measurement variable alone does not provide much information. (14)

d) Culmination Frequency

Nystagmus frequency is the number of beats for a given time period. Culmination frequency (CF) is defined as the number of beats measured within 10 seconds of maximum caloric response. (14) Torok in 1969 argued that culmination frequency shows a smaller standard deviation error than mean peak slow phase velocity (spv). (30) Later on, Kumar (1995) reaffirmed Torok's results (a lesser coefficient of variation in CF compared to that of spv). (31)

e) Mean peak slow phase velocity

Slow phase velocity (spv) is determined by amplitude over time (degrees per second), that is by calculating the slope of the slow phase nystagmus. (3, 14) Mean peak spv is the average spv in a 10 second period of most intense caloric response, unless otherwise specified, as maximum slow phase velocity of one nystagmus would be completely meaningless. (3, 14, 32) Before the advent of computerized systems, mean peak spvs were manually calculated. (32) Nowadays, computerized ENG/VNG systems calculate them automatically. (14) Mean peak spvs are the most useful parameters, inserted in unilateral weakness (UW) (Jongkee's, 1962) and directional preponderance (DP) equations. Mean peak spv shows the greatest sensitivity and the lowest coefficient of variation (38%) among all enlisted parameters (Henriksson, 1956). (3, 14)

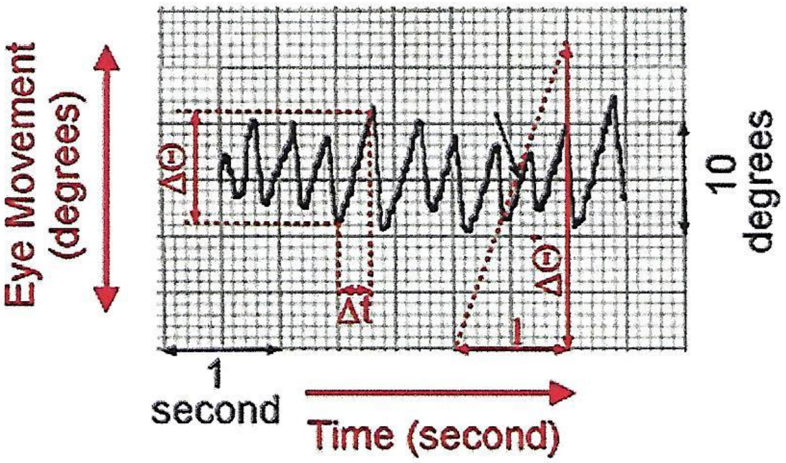

Figure 1. Manual calculation of spv. (Reproduced from Barin). (32)

SPV=ΔΘ/ΔT, SPV=ΔΘ'/1, SPV=slope of line that fits best the slow phase velocity over one second. The scale of X-axis (eye movement of 1 degree is equal to 1 block) and Y-axis (10 blocks represent 1 second) must be known. (35)

Patients Instructions

It is recommended clinical doctors to use simple language and be reassuring to their patients. Interacoustics suggests the following monologue: "I will put warm and cold water/air into your ears. I will begin with your right/left ear. The water/air will feel warm. The water/air will sound loud. You will feel no pain. If you feel any discomfort/pain, please tell me immediately. The water/air will be in your ear for 30/60 seconds. After 30/60 seconds I will take the water/air away from your ear and I will ask you questions. You will feel like you are moving for a while. Please keep your eyes open at all times and when I ask you questions, answer my questions. Do you have any questions? Are you ready to begin the test?" (20)

Recommended procedure (not applicable to babies and very young children) (4, 20)

1) Otoscopy and tympanometry

An otoscopic examination is performed to ensure that the external auditory canal is free of wax that could have any affect in the quality of water or air irrigation and to observe the external auditory canal shape. (20) After that, immittance testing is conducted to show that there is no perforation of the eardrum, not seen by otoscopy. (5) The British Society of Audiology (BSA, 2010) recommends both otoscopic and tympanometric evaluations to be performed before caloric testing and after every irrigation, so that the integrity of the tympanic membrane and of the external ear are checked. (4)

2) Electrooculography (EOG) or videooculography (VOG) preparatory steps.

When EOG is used:

a) Prepare examinee’s skin and attach the electrodes.

b) Perform eye movement calibration in a dim lit environment before every irrigation.

When VOG is used:

a) Place video cameras on examinee’s face.

b) Perform eye movement calibration in a dim lit environment only in the beginning of the caloric test.

Note: Perform monocular EOG or VOG recording in case of any eye abnormality. (14)

3) Caloric irrigation and recording

a) Place the examinee in the standard caloric position (i.e. 30º upward the supine position).

b) Before the first irrigation only, check for any spontaneous nystagmus with or without visual fixation. BSA recommends at that point to record its direction and its average spv.

c) The examinee with eyes open, wearing either Frenzel/video-goggles or in a dim lit environment is told to gaze ahead.

d) Start performing caloric irrigation.

e) Patient’s mental alerting tasks and recording can commence either at the beginning or the end of each caloric irrigation. There should be at least 60 seconds of total recording time after the end of each caloric irrigation.

4) Measurement of caloric-induced and fixation suppression nystagmus

a) Observe caloric-induced nystagmus.

b) Immediately after the peak nystagmus intensity has been reached, fixation suppression commences for a 5-10 second period.

c) After recording ends, perform otoscopy again.

d) Allow at least 7 minutes between the start of individual irrigations (i.e. from start to start). (BSA, 2010) Many laboratories allow a period of 5 minutes. Recent research suggests a minimum period of 3 minutes. During this period calculate mean peak spv and FI.

The British Society of Audiology (BSA, 2010), the American National Standards Institute (ANSI, 1999) as well as Interacoustics suggest the use of VOG over EOG mainly on the basis of calibration, i.e. one calibration for VOG at the beginning of caloric test versus one calibration for each caloric irrigation, a total of four in the case of EOG. (14, 20)

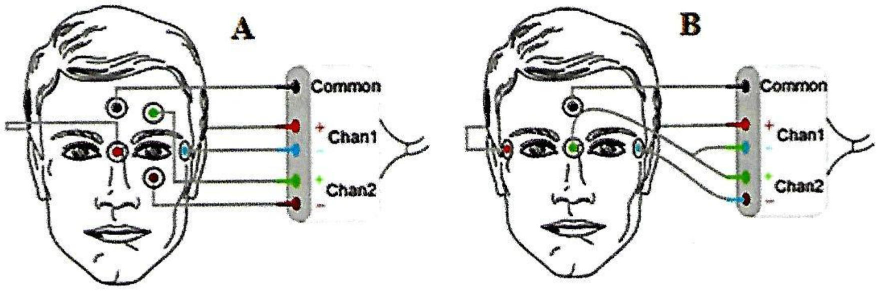

Figure A. Electrodes recording horizontal and vertical left eye movement. Figure B. Electrodes recording horizontal left eye movement. (Reproduced from Barin) (33)

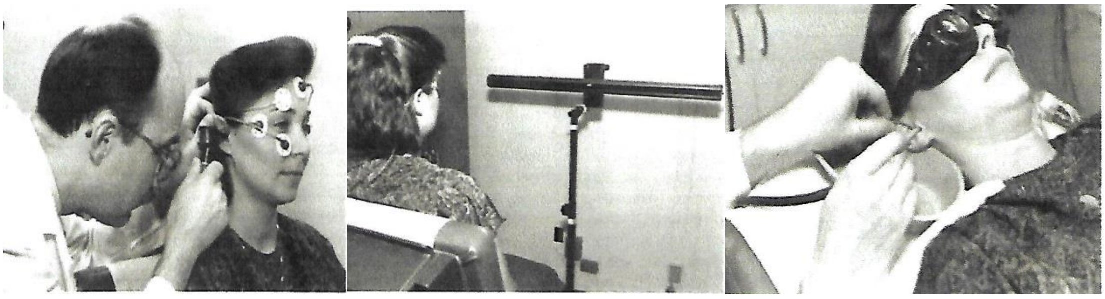

Figure A. Evaluation of external auditory canal and tympanic membrane integrity by otoscopy and tympanometry. Figure B. ENG calibration. Figure C. Caloric irrigation. The patient is 30^{o} above the supine position with eyes open, wearing Frenzel glasses in a semi-lightened environment. (Reproduced from Jacobson) (14)

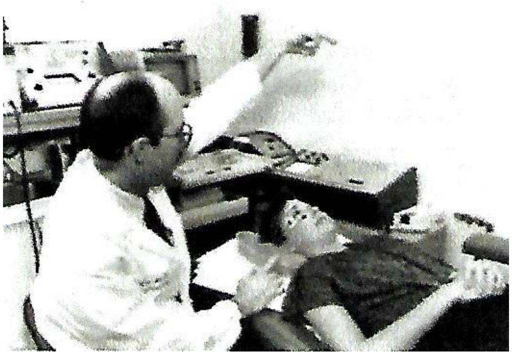

Figure D. Fixation suppression index. Immediately after the peak of caloric response, the patient fixates on the examiner’s finger. (Reproduced from Jacobson) (14)

V. Alternate Binaural Bithermal Caloric Test (ABBT)

The current alternate binaural bithermal caloric test (ABBT) has changed little since it was first described by Fitzgerald and Hallpike in 1942. They placed the patient's head 30° up from supine position (optimal head position of horizontal semicircular canal for caloric stimulation). (14) They conducted the test using an open-loop water caloric irrigator. (5) Each ear was first irrigated with 250 ml of cold water at 30° C within 40 seconds. (14) Since electrooculography (EOG) in 1940s had not been developed, the patient was instructed to keep their eyes open and fixated on a distant target. Latency to the onset of nystagmus (measured in seconds), duration of caloric response (measured in seconds) and direction of the fast phase of nystagmus were taken into account. (5, 14) After some time interval, the irrigation was repeated using 250 ml of hot water at 44° in a time period of 40 seconds. (14) They observed that cold water stimulus produced a fast phase nystagmus beating towards the unstimulated ear, whereas with hot water stimulus, fast phase nystagmus was directed towards the stimulated ear canal (COWS: Cold Opposite, Warm Same; mnemonic rule). (14, 34) Nowadays, electrooculographic or videooculographic recording takes place, so that examiner tracks eye position in a vision-denied environment e.g. patient in complete darkness. (5) A functional semicircular horizontal canal will show caloric response 15 to 30 sec (*15-30 sec) after the start of irrigation and will demonstrate its peak nystagmus intensity after around 45 to 60 sec (*60-90 sec) since water irrigation (*air irrigation) begun. (20)

Test order

The British Society of Audiology (BSA, 2010) recommends that the two warm irrigations be carried out first, followed by the cold ones. Right or left ear does not really matter. This testing order permits the examiner to apply the monothermal caloric screening test (MCST) and then complete ABBT. (4) Clinical doctors may change the order based on clinical findings. (4)

Shepard et al. commence warm irrigation on the external auditory tube of the ear on which they speculate unilateral weakness. Warm irrigations are followed by cold irrigations with the same order. If certain criteria, such as monothermal caloric asymmetry of 10% or less, are met by the two warm irrigations, then they may discontinue further caloric testing. (3)

Lightfoot (2004) failed to report significant systematic bias of the caloric response attributed to the test order of caloric irrigations. (35) Till then, it was common belief among researchers that some form of adaptation took place, thus affecting the spvs obtained from the four caloric irrigations and that indeed the test order could really affect the results. Lightfoot in 2004 showed that corneo-retinal potential change was responsible and that ENG calibration before each caloric irrigation could correct it. (35) When videonystagmography was used, no significant habituation was observed. (35) Proctor et al. did show that corneo-retinal potential decreases over time (a 7% decrement over a period of 8 irrigations). They speculated that darkness is the cause as the value of corneo-retinal potential is greatest in a well-lighted environment. (36) Jacobson et al. reported that the first caloric stimulus usually causes the largest caloric response. This observation is attributed to a) extra mental concentration in the beginning of the test as the patient is not familiar with the test, b) some form of habituation after repeated irrigations and c) corneo-retinal potential changes over time. They suggested that ENG calibration preceding each irrigation should be performed and light in the examination room to be kept constant (no turning on/off of lights during caloric testing). (14) Lightfoot et al. (2009) proposes that ABBT when certain criteria are met, can be terminated after the first two warm full irrigation cycles have been conducted. (28)

In our opinion, the examiner should start with warm irrigation on the external ear canal of the ear on which unilateral weakness is speculated. Warm irrigations are followed by cold ones with the same order, that is, the suspect ear is examined first. The aforementioned test order permits the examiner to apply the monothermal caloric screening test (MCST) criteria set by BSA and based on clinical grounds to conclude the test if deemed necessary.

Parameters of ABBT stimuli (tables 1 and 2)

Open- and closed-loop water and air caloric irrigation parameters recommended by the American National Standards Institute (ANSI), and British Standards Association (BSA) to generate equivalent responses

	Most commonly reported in literature			ANSI (1999) recommended			BSA (1999) recommended		
	Open-loop water	Air	Closed-loop water	Open-loop water	Air	Closed-loop water	Open-loop water	Air	Closed-loop water
Volume	250 mL	8 liters	–	200±20 mL	X	350±35 mL	250±10 mL	8±0.4 liters	X
Duration	30 seconds	60 seconds	45 seconds	40±1 seconds	X	40±1 seconds	30 seconds	60 seconds	X
Temperature (warm/cool)	44/30°/C	50/24°/C	46/28°/C	44/30±0.5 °/C	X	44/27°/C	44/30±0.4 °/C	50/24±0.4 °/C	X

Table 1. Reproduced from Shephard. (3)

British Society of Audiology (2010): open-loop water and air caloric irrigation parameters.

	Temperature: 'cold'	Temperature: 'warm'	Flow rate
Water	30 °C ± 0.4 °C	44 °C ± 0.4 °C	250 ml ± 10 ml in 30 s
Air	24 °C ± 0.4 °C	50 °C ± 0.4 °C	8 l ± 0.4 l in 60 s

Table 2. Reproduced from British Society of Audiology. (4)

Note: British Society of Audiology (2010) suggests that laboratories using air irrigators should collect their own normal values because air caloric performance depends on flow rate, temperature and speed of air delivered (diameter of delivery tip).

Parameters Calculation from ABBT

a) Unilateral Weakness (UW)

The percent reduced vestibular response (%RVR) (ANSI,1999) is calculated using the Jongkee's formula. (3, 37)

$$UW = \frac{(RW + RC) - (LW + LC)}{RW + LW + RC + LC} \times 100$$

Unilateral Weakness (UW) equation (Jongkee's formula). RW: right ear, warm irrigation. RC: right ear, cold irrigation. LW: left ear, warm irrigation. LC: left ear, cold irrigation. Reproduced from Bahner. (37)

The formula above compares caloric responses of one ear with those obtained from the other, i.e. symmetry of right and left vestibular function. (3, 37, 38) Most laboratories set %RVR normative value lower than 20-25% as this range corresponds to the mean of +/-1.96 standard deviations. (3, 4) An asymmetry greater than 20-25% indicates unilateral reduced vestibular reaction of the ear eliciting the weaker response. (37) Jongkee's formula is solely based on caloric-induced spvs as spontaneous nystagmus spvs cancel out, therefore arithmetic correction for spontaneous nystagmus is needless. (4, 39)

b) Directional Preponderance (DP)

Fitzgerald and Hallpike in 1942 were the first to address the issue of clinical significance of directional preponderance, even though the equation calculating it, was formulated by Jongkees and Philipson in 1964. (40) Sixty years later, DP's clinical relevance is still controversial and debated. (14, 39) DP value compares the intensity of right directed nystagmus to that of left beating nystagmus. (20) Most researchers consider any DP value lower than 30^o /sec within the normative range. (3, 20, 37) DP in the vast majority of cases is seen in patients presenting spontaneous nystagmus, producing a baseline shift. (39) Subjects with central or peripheral vestibular lesions, cortical injuries or even healthy may present DP exceeding normative values. (40) To sum up, DP alone does not correlate with vestibular disease and does not localize the lesion. (40) The aforementioned issues have driven many researchers to claim that DP has little if any clinical significance. (38)

Most renounced researchers stress out that DP can not be interpreted alone. In case there are signs of central vestibular dysfunction, DP is rather produced by central system lesion. If no central system abnormalities can be found, then DP is indicative of a biased peripheral vestibular response not compensated for centrally. (Halmagyi, Shephard, Jacobson, Eggers and Barin) (3, 39)

$$DP = \frac{(RW + LC) - (LW + RC)}{RW + LW + RC + LC} \times 100$$

Directional Preponderance (DP) equation. RW: right ear, warm irrigation. RC: right ear, cold irrigation. LW: left ear, warm irrigation. LC: left ear, cold irrigation. Reproduced from Bahner. (37)

Notice: when calculating UW and DP using the aforementioned formulas, corrections for any spontaneous nystagmus should not be made. (4) Most systems nowadays calculate UW and DP automatically. (4)

c) Baseline Shift (BS) and d) Gain Asymmetry (GA) DP

$$DP = \frac{TotRB - TotLB}{TotRB + TotLB} \times 100$$

$$TotRB = -PeakRW - PeakLC = -CalRW - CalLC - 2SN$$

$$TotLB = PeakRC + PeakLW = CalRC + CalLW + 2SN$$

DP denotes directional preponderance. TotRB: total responses causing right-directed nystagmus, TotLB: total responses causing left-directed nystagmus, PeakRW: spv for right ear, warm irrigation, PeakLW: spv for left ear, warm irrigation, PeakRC: spv for right ear, cold irrigation, PeakLC: spv for left ear, cold irrigation. (39)

Peakxx = Calxx + SN

where Cal stands for spv of caloric-elicited nystagmus, SN: spv of spontaneous nystagmus and XX: RW, LW, RC and LC. (39)

$$DP = \frac{-4SN}{(-CalRW - CalLC) + (CalRC + CalLW)} + \frac{(-CalRW - CalLC) - (CalRC + CalLW)}{(-CalRW - CalLC) + (CalRC + CalLW)} \times 100$$

$$DP = \frac{-4SN}{(-CalRW - CalLC) + (CalRC + CalLW)} + GA$$

$$GA = \frac{(-CalRW - CalLC) - (CalRC + CalLW)}{(-CalRW - CalLC) + (CalRC + CalLW)} \times 100$$

Note. In the above formulas the assigned spv values are: positive for right slow phase nystagmus (left-beating) and negative for left slow phase nystagmus (right-beating).

In case nystagmus observed has an opposite direction than expected, as long as the correct signs for spv are used, the above equations still hold true.

Spontaneous nystagmus is added to caloric-elicited nystagmus when they both have the same direction and subtracted when they have opposing directions. (39)

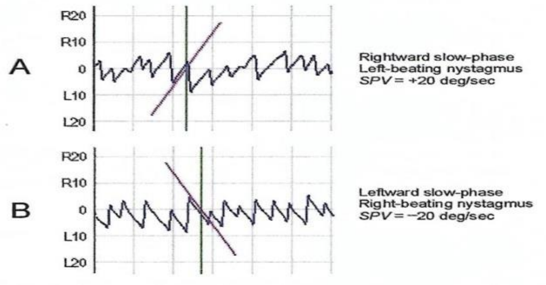

Figure A. Positive sign for right spv values (left-directed nystagmus). Figure B. Negative sign for left spv values (right-directed nystagmus). Reproduced from Barin. (39)

There are two types of DP: a) baseline shift (BS) accounting for the spontaneous nystagmus and b) gain asymmetry (GA) accounting for the true asymmetry between right beating versus left beating nystagmus when baseline shift (spontaneous nystagmus) is equal to zero. (3, 39) Baseline shift (BS) DP is encountered in 99% of cases when DP exceeds normative range, while Gain Asymmetry (GA) DP is found in the rest. (Halmagyi et al., 2000) (39) Baseline shift (BS) is quantified using the average spv of nystagmus during the first seconds of each caloric irrigation, while Gain Asymmetry (GA) is calculated solely upon caloric-elicited nystagmus spv. (39) Baseline Shift (BS) normative value is < 4-6º /sec, while Gain Asymmetry's < 25% (according to Halmagyi < 40%). (39) Baseline shift (BS) refers to the direction of peak spv, while Gain Asymmetry to fast phase direction. (39)

e) Bilateral Weakness

Bilateral weakness (BW) is defined as absent or decreased function of both labyrinths. BW etiologies vary remarkably (idiopathic 51%, ototoxicity and metabolic disorders 13-21%, infectious diseases 3.8-12%, autoimmune diseases 10%). (41) Its main symptoms are: a) oscillopsia, and b) chronic unsteadiness. (41) Patients with severe bilateral weakness will experience limitations in their daily activities, e.g. refrain from driving. (42) Most patients with mild BW within 1-2 years will show a considerable improvement. (42)

Caloric test is used to identify BW. Total caloric response is the sum of absolute values of mean peak slow phase velocities, appropriately directed. (37, 38) In case of spontaneous nystagmus, caloric responses are corrected. The sum of absolute values of all four caloric responses is calculated (RW and LC right beating, RC and LW left beating). If a response direction is opposite than normally expected, this caloric response is subtracted from the other three. (38) Bilateral weakness is present when the total caloric response has a value of 20-25º /sec or less. (37, 38) Zapala et al. (2008) reported that one person in a hundred will show a total caloric response (total eye speed) of less than 27º /sec. (42) While this criterion, i.e. a value of <20-25º /sec shows a considerable specificity, still patients on the borderline of bilateral canal paresis can be missed. (41) BW incidence rate in caloric test varies from 0.6-13.6%. (41)

TR = (RC + LC +RW + LW)

Total caloric response equation. RC: right ear, cold irrigation. LC: left ear, cold irrigation. RW: right ear, warm irrigation. LW: left ear, warm irrigation. Reproduced from Hain. (38)

Stockwell (1993) reported that a caloric response from each ear lower than 12º /sec is indicatory of bilateral weakness. (3) The Barany Society Consensus document uses a stringent diagnostic criterion, i.e. the sum of warm and cold irrigations from each ear less than 6º /sec. (42) The British Society of Audiology (BSA, 2010) recommends that bilateral hypofunction may be inferred if all four mean peak spvs are lower than 8º /sec. (4) It stresses out that even though the value of 8º /sec represents the 95% confidence interval of median of all four irrigation, the 95% confidence interval of each irrigation has a range between 5º/sec to 57º/sec. (4)

Some researchers have reported a sensitivity of just 64.6% of caloric testing reporting bilateral weakness. (41) False negatives are due to the wide range of caloric responses in healthy subjects, that is, healthy individuals showing a response of more than two standard deviations. (3, 42) False positives may be due to ear anatomy variations (e.g. narrow external auditory tubes), the presence of wax, no correction of caloric response values for age or weak caloric stimulus (e.g. air caloric irrigation). (41, 42) In case caloric testing reports bilateral weakness, rotatory chair testing (ROT) should confirm it as caloric testing represents a low frequency sinusoidal wave of 0.003 Hz compared to 0.01 Hz of ROT. If ROT is normal, then caloric response values obtained for BW are considered normal too. (3, 14, 37, 38, 41)

f) Hyperactivity

Hyperactive caloric response is observed in cases of increased excitatory state of vestibular neurons in central nervous system. It is believed that decreased cerebellar inhibition plays a crucial role. (43) It is almost always a bilateral phenomenon. It is encountered in less than 1 in 1000 caloric tests. (44) In an anxious patient undertaking caloric test, hyperactivity may be observed. (45)

Barber et al. (1980) considered caloric responses hyperactive if mean peak spv is greater than 80º /sec for each warm irrigation and/or greater than 60º /sec for each cold irrigation respectively. (10) Jacobson et al. (1993) reported that hyperactivity could be assumed if the sum of warm irrigations was larger than 146º /sec and/or larger than 99º /sec the sum of cold irrigations and/or a total of at least 221º /sec all four caloric irrigations. (3) Bahner et al. (2013) suggested that the sum of warm and cold irrigations from the right or left ear should exceed 140º /sec, so that hyperactivity may be considered. (37) Barin supported that all four irrigations should be larger than 80º /sec. In case, when one or two irrigations are greater than 80º /sec, this finding does not support hyperactivity and a possible artifact or strong spontaneous nystagmus may have been accumulated. Repetition of irrigation is deemed necessary to clarify the situation. (44) When caloric responses from one ear are found hyperactive, a possible explanation may be that the patient has a central lesion on that side as well as a peripheral one on the opposite side of weakness. (44) Over-calibration and a breach in the integrity of the ear drum should be ruled out. (44) Air calorics have been occasionally reported to elicit very strong responses when applied on perforated tympanic membrane. (44) In doubtful cases, rotatory chair testing is undertaken in order to confirm hyperactivity. (3)

g) Fixation Index

The Fixation suppression Index (FI) examines the vestibulo-ocular reflex integrity. (3, 46) It is expressed as the ratio of nystagmus intensity for a time period after fixation and nystagmus intensity for a time period before fixation, expressed as percentage (ANSI, 1999). FI is calculated for the right direction of nystagmus (FI RB) and for the left direction of nystagmus (FI LB), therefore FI is carried out for two irrigations of the same temperature (more often warm irrigations) from a total of four. (4, 37, 46) In case, fixation merely suppresses nystagmus, FI values will be ranged from 0 to 100%. If nystagmus is completely suppressed by fixation, then FI value will be equal to 0% and the opposite, a fixation index of 100% indicates no fixation. It is obvious that if fixation enhances nystagmus, then FI will be greater than 100%. (37, 46)

It is strongly recommended that fixation suppression commences immediately after the peak nystagmus intensity has been reached. (37, 46) McCaslin showed that if the patient fixates long after nystagmus intensity peak, the test may become invalid. (37) Kato et al. found that FI obtained from a strong caloric response is more informative than that obtained from a weak nystagmus intensity. (14) Barin suggests visual fixation to be initiated 40-45 seconds after caloric irrigation ends. Nystagmus beats one second before as well as one second after visual fixation should be discarded as artifacts during this period may be present. (46) A 5-second period before and after fixation is recognized and spvs of 3 nystagmus beats are measured for each period. The averages are used in the following equations to calculate FI. (46)

$$\text{FI RB} = \frac{\text{Fix RW or LC}}{\text{NoFix RW or LC}} \times 100$$

where FI RB denotes fixation suppression index for right-directed nystagmus response, Fix: with fixation, NoFix: no fixation, RW: right ear, warm irrigation, LC: left ear, cold irrigation. (37)

$$\text{FI LB} = \frac{\text{Fix LW or RC}}{\text{NoFix LW or RC}} \times 100$$

where FI LB denotes fixation suppression index for left-directed nystagmus response, Fix: with fixation, NoFix: no fixation, LW: left ear, warm irrigation, RC: right ear, cold irrigation. (37)

British Society of Audiology (BSA, 2010) uses an alternative formula for calculating the visual fixation index (VFI):

$$\text{VFI} = \frac{2V_2}{V_1 + V_3} \times 100\%$$

where V_1 stands for spv average or representative value over a period of 5 seconds preceding visual fixation, V_2 during fixation and V_3 for a period of 5 seconds immediately after. (4)

Researchers disagree on which values are normative. (4, 37, 46) Demanez et al. (1970) reported FI lower than 50% to be considered normal. Alpert suggested that the normal range was between 60 to 70%. Jacobson et al (1993) considered FI values lower than 60% as normative. Most laboratories accept any value lower than 50 to 60% as normal, i.e. healthy subjects and patients will have a FI value less than 50-60%. Any values greater than 50-60% are considered pathological and indicative of a central vestibular lesion. (3, 4, 37, 46) The localization of the central lesion can be in the cerebellum (midline), the parietal-occipital cortex and the pons. (46)

The British Society of Audiology (BSA, 2010) and Barin (2007) suggest that patient's visual acuity is an issue when performing the fixation suppression test. (4, 46) BSA reports that VFI calculation is meaningless when nystagmus with fixation is abolished. In patients with weak nystagmus, i.e. with bilateral vestibular weakness, FI will not be considered valid. (46) Normal FI values are observed in patients with unilateral peripheral vestibular lesions (labyrinth or vestibular nerve lesions). (46) Finally, patients with normal vestibular function, but pathological oculomotor function may have normal or pathological FI, the latter more commonly found, depending on localization of oculomotor lesion. (46)

Fixation Index test suffers from certain limitations: a) Optimum spvs before fixation have a range between 20 to 40º /sec. If spvs are below 20º /sec, examinees may voluntarily suppress nystagmus. b) Fixation suppression is dependent on subject's age and gender (Jacobson et al., 1993). Till now, there is no age or gender-adjusted fixation suppression index. c) Visual fixation is under examinee's voluntary control. A patient unwilling to participate in the test will come with an invalid FI value. d) Fixation suppression shares common mechanisms with the pursuit system, thus few patients with a pathological smooth pursuit test will show a normal vestibulo-ocular reflex suppression. (46)

Clinical doctors immediately after the peak of nystagmus intensity will instruct the patient to gaze at a fixed point (e.g. examiner's finger or a LED light in Frenzel or VNG goggles). (3) Examiner's direct observation and patient's willingness to participate in the test are prerequisites. (46)

Results reporting

Most laboratories do not report which medium (water or air) and which type (open or closed-loop systems) were used to conduct caloric irrigations. Water surpasses air in eliciting a more intense caloric response. (28) If either electrooculography or videooculography were employed, it should be stated. Tympanic membrane perforation and/or middle ear surgery should be included in the statement as these conditions permit only to determine if vestibular response is present or not. (20) UW value corresponds to the weaker side of peripheral vestibular function. (4) DP refers to the fastest nystagmus direction elicited by caloric testing. (4) In cases where bilateral weakness is observed, UW and DP will not be calculated. (20) The lowest absolute value of mean peak spvs for all four irrigations not confounding UW and DP is 6º /sec. (4) Normative values of caloric response parameters should be explicitly stated. BSA recommends that each laboratory establishes its own normative values, especially in the case of air calorics. (4)

Normative values for caloric response (ABBT) parameters

Parameter	Common[1]	BSA[2]	Alternative[3]
Unilateral Weakness (UW)	< 25%	< 20%	< 20-30%
Directional Preponderance (DP)	< 30%	< 20%	< 25-50%
Baseline Shift (BS)	< 4 – 6^o /sec		
Gain Asymmetry (GA)	< 25% [4]		< 40% [5]
Bilateral Weakness	Total mean peak spv from each ear > 12^o /sec (i.e. RW+RC > 12^o /sec and LW+LC > 12^o /sec)	Mean peak spv from each caloric irrigation > 8^o /sec (i.e. RW, LW, RC, LC > 8^o /sec)	Sum of right and left ear mean peak spvs > 22-30^o /sec (i.e. RW+RC+LW+LC > 22-30^o /sec
Hyperactivity	Total mean peak spv from right ear < 140^o /sec (i.e. RW+RC < 140^o /sec) AND/OR Total mean peak spv from left ear < 140^o /sec (i.e. LW+LC < 140^o /sec)		Individual mean peak spv of right warm and left warm irrigations < 80^o /sec (i.e. RW< 80^o /sec and LW< 80^o /sec) AND/OR Individual mean peak spv of right cold and left cold irrigations < 50-60^o /sec (i.e. RC< 50-60^o /sec and LC< 50-60^o /sec)
Fixation Index (FI)	< 50%	< 50%	< 50-70%

1. Interacoustics (Jacobson et al.). 2. British Society of Audiology (2010). 3. Others. 4. Barin. 5. Halmagyi.

Note. According to British Society of Audiology, when mean peak spvs for all four caloric irrigations are ≤ 5^o /sec, then UW and DP can not be calculated (systematic errors will approximate the absolute values). (4)

VI. Ice Water Caloric Test (IWCT)

When there is a weak response or no response to the ABBT, unilaterally or bilaterally, ice water irrigation to verify the presence of any residual function is deemed necessary. (3, 4, 5, 14) The IWCT is conducted in a visual fixation denied environment (as the ABBT) with the patient's head inclined to one side, so that the test ear faces upward. (3, 4, 5, 14) Two milliliters of iced water drawn from a syringe are infused into the ear canal over a period of 5 to 10 seconds. (3, 4, 5, 14) The iced water is obtained from a cup filled with water and ice cubes. (4, 14) It should have a low temperature. (3, 4, 5, 14) Jacobson et al. suggest that a temperature of 10^{o} C suffices. (14) In any case, prior to infusion with a syringe, the iced water temperature is recorded. (4) After 20 to 30 seconds the patient's head returns from the semi-recumbent position to the standard supine position (30^{o} up from horizontal plane), thus dumping the cold water out of the ear canal. (3, 4, 5, 14) Electrooculography (EOG) recording begins with the patient instructed to perform mental alertness tasks. (4, 14) In cases when spontaneous nystagmus exists or controversial readings have been obtained, it is suggested that the patient be placed in the prone position, after nystagmus has commenced in the standard supine position (patient's head and body inversion 180 degrees). (Shepard et al., Jacobson et al.) (3, 14) Bhansali et al. suggest that in cases of bilateral paresis, contradictory results or spontaneous nystagmus, ICWT should be performed not only in the standard supine position, but also in the prone position. (5) The British Society of Audiology (BSA) guidelines do not offer any insight as ICWT is terminated in the supine position. (4) The rationale of performing two additional iced water irrigations in the prone or supine/prone position is that a cold stimulus in the prone position (ampullopetal deviation of the cupulla) will evoke a stronger response than in the supine position (ampullofugal) in accordance to Ewald's law. (3, 5) Also, if any spontaneous nystagmus exists in the supine position, no direction reversal will be observed when the head assumes the prone position. (3, 14) Shepard et al. suggest that rotatory chair test should follow when the clinical doctor suspects a complete bilateral weakness. There is empiric evidence that it is possible middle or high-frequency function to exist while there is no residual low-frequency function. (3)

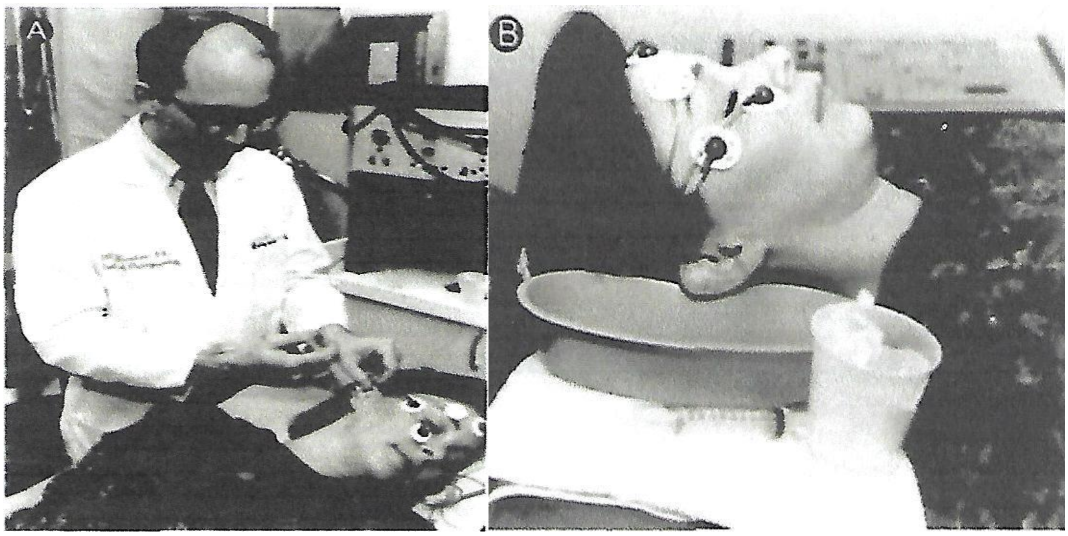

Figure A. Patient's head facing upward for a 2 ml infusion of iced water. Figure B. Patient in the standard supine position (30^{o} up from the horizontal plane). (Reproduced from Jacobson). (14)

VII. Monothermal Caloric Screening Test (MCST)

Monothermal caloric test (MCT) was first proposed by Bernstein and Hart in 1965 in an effort to reduce time, cost and discomfort of patients undergoing vestibular evaluation. Barber et al. in 1971 reported a low false-negative rate of only 7% when response difference between the two labyrinths was larger than 25% and the nystagmus caused by each irrigation produced a slow phase velocity of 11 degrees per second or greater. They also reported that the warm caloric stimulus had a better predictive value (less false negative results) than the cold one, thus enabling to replace the ABBT. (3) Becker in 1979 found a 22% false-positive rate and a 14% false-negative rate when using Barber et al. criteria, comparing warm MCT with ABBT. Overall, the two tests showed a 77% agreement on the caloric response difference. It is still unclear why monothermal cold caloric test shows more false negative results than the warm one. Certain researchers have suggested that it is more advantageous to evaluate the function of the vestibular organ at levels above its spontaneous discharge rate (warm stimulus), rather than at levels closer to its lower functional limits (cold stimulus). (14) Jacobson et al. in 1985 and in 1995 showed that the performance of monothermal warm caloric test improved if the rest of ENG test battery was normal (positional and positioning tests as well as visual-oculomotor function tests). They found that the false-negative rate dropped to 5-6% when using 30% caloric response asymmetry, spv of 11 degrees or greater and all subtests of ENG were normal. (3)

Lightfoot et al. in 2009 proposed three criteria yielding a MCST sensitivity of 95% (false-negatives 5%) and specificity 71% (false-positives 29%): a) monothermal warm caloric asymmetry < 15%, b) spv > 8^o /sec and c) spontaneous nystagmus < 4^o /sec. Water or air mediums performing stimulation did not influence test results, thus they were considered irrelevant, even though with water a more sustainable temperature difference was obtained. (28)

Adam et al. in their systematic review in 2016 suggested that for the standard ABBT unilateral weakness threshold (UW>20 or UW>25), a low monothermal warm caloric asymmetry (MWCA) cutoff of 15% and a spv of 11 degrees or greater would result in less than 5% false-negatives and would reduce the need of ABBT by half. MWCA value should not exceed the cutoff values as MCST would be impossible to discriminate between unilateral weakness or directional preponderance based on two warm irrigations. (14) They noted that any oculomotor findings, spontaneous or positional nystagmus, as well as weak caloric responses should prompt ABBT administration. (16)

The established MCST criteria of British Society of Audiology (BSA) published in 2010 are the following: a) MWCA < 15%, b) spv > 8^o /sec for each irrigation to exclude the possibility of bilateral weakness and c) spontaneous nystagmus mean/maximum spv < 4^o /sec. If the above criteria are not met, then the complete ABBT should be performed. BSA does not recommend the cold MCT. (4)

To summarize, most researchers agree that caloric testing should begin with warm water or air irrigations. If the examinee is unable or unwilling to complete the ABBT, then MCT following certain criteria may predict with high accuracy if ABBT would have been normal or not. Overall, MCT as a screening test does not work well in the borderline of normal and abnormal vestibular function, that is why, it is recommended to complete the ABBT when this is possible. (3, 47)

$$MWCA\ \% = (R - L) / (R + L) \times 100$$

Formula for determining asymmetry of function. MWCA: monothermal warm caloric asymmetry, R: right peak slow phase velocity of nystagmus, L: left peak slow phase velocity of nystagmus. Reproduced from Adams. (47)

VIII. Simultaneous Binaural Bithermal Caloric Test (SBBT)

In an attempt to yield caloric responses demonstrating greater sensitivity than those achieved by ABBT, Brookler in 1971 described the simultaneous irrigation of both external ear canals with cold and then warm water using a closed-loop irrigation system (a "Y" tube). Each single water irrigation had an output of 250 ml and was delivered in 30 seconds. Cold water irrigation was at 30º C and hot water at 44º C respectively (same temperatures as in ABBT). There was a 5 minute interval between the two irrigations. (14, 25) Conventional electrooculography was used to record the caloric nystagmus for 60 to 90 seconds since the onset of caloric irrigation. (14, 25) The patient was placed in the 30º supine position as in ABBT. (25) The rationale for this test was that if both vestibular organs function symmetrically, no nystagmus should be observed as both labyrinths are stimulated in an equal but opposite way, thus canceling each other. (48)

SBBT has no quantitative measurements. The presence or absence of caloric nystagmus as well as its direction following each irrigation are recorded. (14) These result in 4 types of responses with 9 combinations. (27)

Type I response corresponds to no nystagmus observed, either with warm or cold caloric stimuli. It is indicative of normal function, but can be seen in bilateral labyrinth weakness or irritation. (48)

Type II responses are those in which the direction of nystagmus reverses with each irrigation. In cases when there is unilateral hypofunction or unilateral hyperactivity, vestibular lesion can be identified as warm stimulus will elicit nystagmus beating away from the weaker side, while cold stimulus will cause nystagmus to be directed towards the weaker side. (48) According to Bookler, type II responses correspond to reduced vestibular response (UW). (27)

Type III response corresponds to nystagmus beating in one direction regardless of warm or cold irrigations. It indicates a directional preponderance (DP), possibly incited by spontaneous nystagmus (Brookler). (48)

Type IV response is one in which nystagmus is elicited by one caloric stimulation, but not by the other. (48) Bookler describes it as a nonspecific anomaly as the vestibular lesion can not be located. (27)

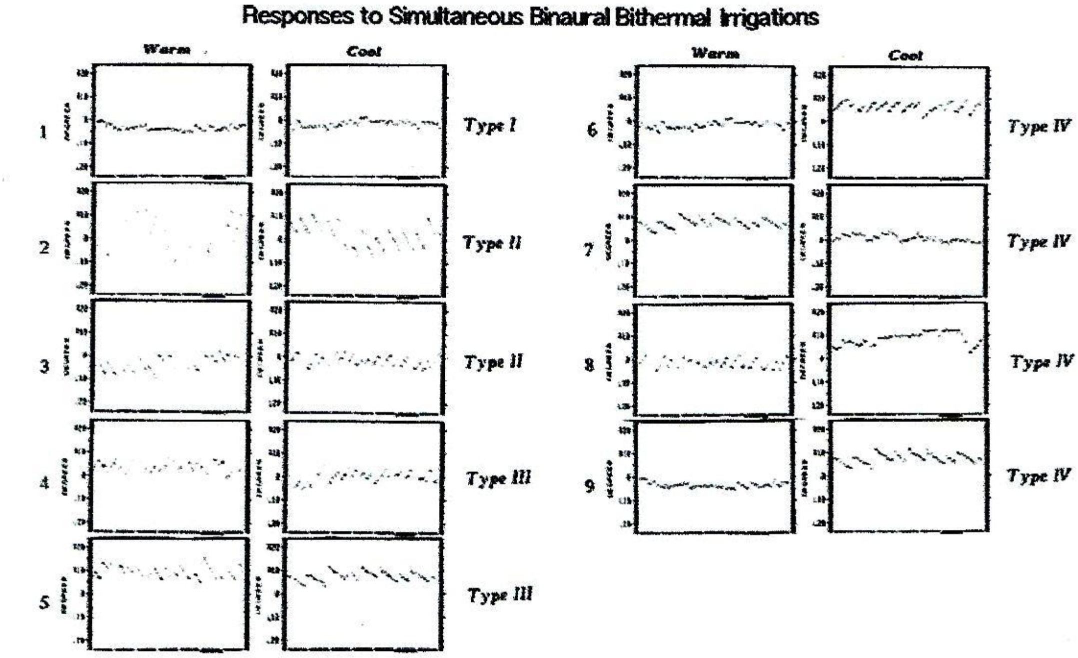

Figure 1. The four types of responses and the nine combinations from the simultaneous binaural bithermal caloric test (SBBT). (Reproduced from Furman). (27)

Brookler's research in 1971 and 1975 showed that SBBT has a higher sensitivity than ABBT and should be used in conjunction with ABBT. Adding another six and a half minutes (SBBT duration), sensitivity improves by 55%. (25, 26) Furman et al. study in 1988 found that SBBT was more sensitive, but ABBT was more specific. ABBT was found to distinguish better a healthy subject from a patient subject. The two tests showed poor agreement. When the two tests were combined, rather than using the ABBT alone, there was no improvement in distinguishing a healthy population from a patient one. (27) Salatoff et al. in 2017 proposed that SBBT should be performed in cases peripheral vestibular pathology is suspected clinically, but not confirmed by ABBT, as SBBT has a better sensitivity than standard ABBT. (48)

SBBT is an adjunct test and in no case can replace ABBT. (14, 25, 48) SBBT is a totally different test than ABBT, based on different principles and correlates poorly with it. (27) It excites or inhibits both the right and the left horizontal semicircular canals. There is no physiologic stimulus exciting or inhibiting both labyrinths at the same time. Therefore, the terms UW and DP should be cautiously used as they are not directly comparable to the ones from ABBT. SBBT can identify either UW or DP, but not both as ABBT does. When nystagmus has a very low amplitude, then ambiguous results arise. The direction of nystagmus may change if the time course of the caloric response between the two labyrinths is different. With SBBT the clinical doctor does not have the opportunity to judge on a discrepancy and therefore repeat an irrigation, as with ABBT. (27) Overall, SBBT is not easily performed and the interpretation of its results requires clinical expertise.

IX. Caloric test indications and findings in certain disorders

Caloric testing is used: a) to confirm that vertigo is of peripheral vestibular etiology, ruling out central one. (49) However, we should bear in mind that in up to 25% of cases, it failed to aid clinical doctors to draw any conclusions. (2) A normal caloric testing does not mean a typical vestibular function. It is reported that up to 35% of patients suffering from dizziness of peripheral vestibular etiology will have normal caloric test findings. (50) b) It offers doctors and patients better understanding and reassurance of a definite diagnosis. (49) c) A specific treatment plan including vestibular rehabilitation may be undertaken. (49) d) In case of labyrinthectomy, the presence of vestibular function of the opposite labyrinth must be assessed, so that no oscillopsia will result. e) Caloric-induced nystagmus in a comatose patient indicates an intact brainstem. (49) f, g) Vestibular neuritis (superior) and ototoxicity (e.g. aminoglycoside) are documented objectively. (7, 51)

A proposed strategy is to perform ABBT when there is a high pretest probability of peripheral lesion, whereas, MCST when there is a high suspicion for central etiology. In case MCST is negative (symmetric caloric responses), then terminate the test and order neuroimaging tests (e.g. MRI). (49) We should stress out that the aforementioned strategy covers enough cases of vertigo, but not all. For example, a vestibular schwannoma can elicit a pathological caloric response, i.e. unilateral weakness indicatory of peripheral vestibular dysfunction, but still, the lesion to be a central one. Caloric testing alone can not exclude vertigo of central etiology.

Commonly encountered vestibular disorders, tumors and trauma

1) Vestibular neuritis (superior)

Unilateral weakness (UW) will be found in caloric testing. (51)

2) Vestibulotoxicity

Caloric responses will be absent or weak, giving notion to bilateral weakness. (51)

3) Meniere’s disease

At the beginning of vertigo spell, spontaneous nystagmus will beat towards the affected ear, while at the end of the spell, towards the healthy ear. In the long-term, 33 to 66% of patients will show unilateral weakness (UW) of the affected ear. (52)

4) Vestibular migraine

Various studies have shown abnormal caloric test results ranging from 22 to 44% in this group of patients. (53)

5) Vestibular schwannoma

Caloric testing has been replaced by Auditory Brainstem Response (ABR) and MRI scanning. It is still useful in cases where small schwannomas reside in internal auditory canal for choosing surgical approach or predicting patient’s vertigo after surgery. (5)

6) Perilymphatic fistula

Caloric testing can be normal or pathological.

7) Head and neck trauma

Certain studies report that up to half of patients suffering from dizziness following trauma will show reduced caloric responses. (54)

8) Multiple sclerosis

In case cerebellar flocculus is affected by multiple sclerosis, then bilateral weakness will be observed. (45) If the floor of the fourth ventricle in brainstem is affected, then caloric perversion, i.e. vertical instead of horizontal nystagmus during caloric testing will be noticed. (45)

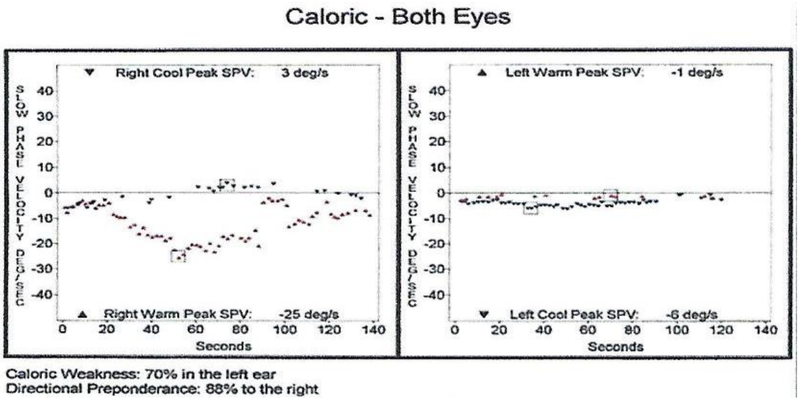

Figure 1. An example of unilateral weakness (UW) of left labyrinth. The most common cause is vestibular neuritis. Reproduced from Hain. (51)

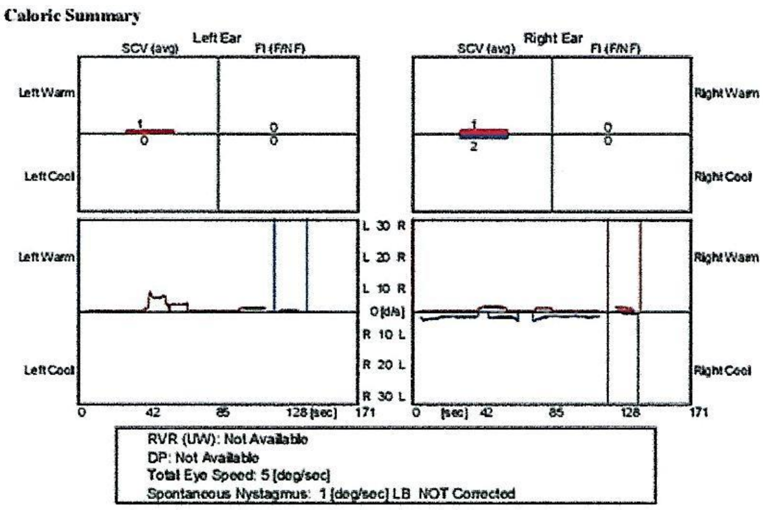

Figure 2. An example of bilateral weakness. The most common causes are poor ENG technique (e.g. wrong placement of electrodes, air irrigation) and after that ototoxicity (e.g. aminoglycoside). Reproduced from Hain. (51)

Normative values for caloric response (ABBT) parameters, clinical significance and common clinical entities

Parameter	Common	BSA	Alternative	Clinical significance	Common clinical entities
Unilateral Weakness (UW)	< 25%	< 20%	< 20-30%	Peripheral or central lesion	Vestibular neuritis, Meniere's disease, Acoustic neuroma
Directional Preponderance (DP)	< 30%	< 20%	< 25-50%	Little clinical significance (healthy subjects, peripheral or central lesion)	
Baseline Shift (BS)	< 4 – 6º /sec			Spontaneous nystagmus	
Gain Asymmetry (GA)	< 25%		< 40%	DP=GA when no spontaneous nystagmus	
Bilateral Weakness	Total mean peak spv from each ear > 12º /sec (i.e. RW+RC > 12º /sec and LW+LC > 12º /sec)	Mean peak spv from each caloric irrigation > 8º /sec (i.e. RW, LW, RC, LC > 8º /sec)	Sum of right and left ear mean peak spvs > 22-30º /sec (i.e. RW+RC+LW+LC > 22-30º /sec	Poor ENG technique (e.g. wrong electrodes, air irrigation), ototoxicity, central lesion, systemic infections, metabolic diseases, no cause in 20%	Ototoxicity: gentamycin, cinnarizine, flunarizine. Systemic infections: congenital/acquired syphilis Central lesion: supratentorial tumors, benign intracranial pressure, Friedreich's ataxia Metabolic diseases: Wernicke-Korsakoff's encephalopathy, Cogan syndrome
Hyperactivity	Total mean peak spv from right ear < 140º /sec (i.e. RW+RC < 140º /sec) AND/OR Total mean peak spv from left ear < 140º /sec (i.e. LW+LC < 140º /sec)		Individual mean peak spv of right warm and left warm irrigations < 80º /sec (i.e. RW< 80º /sec and LW< 80º /sec) AND/OR Individual mean peak spv of right cold and left cold irrigations < 50-60º /sec (i.e. RC< 50-60º /sec and LC< 50-60º /sec)	Central, peripheral (rarely), anxiety, mastoidectomy, tympanic membrane perforation/atrophy/ retraction, overcalibration	Almost always Bilateral: anxiety, central lesion (e.g. multiple sclerosis) Rarely Unilateral: peripheral, central (contralateral labyrinth to that with a deficient response), mastoidectomy, tympanic membrane perforation/atrophy/retraction
Fixation Index (FI)	< 50%	< 50%	< 50-70%	Healthy subjects/peripheral or central lesion	Central lesion: cerebellum (midline), parietal-occipital cortex, pons.

Note. According to British Society of Audiology: a) when mean peak spvs for all four caloric irrigations are ≤ 5º /sec, then UW and DP can not be calculated (systematic errors will approximate the absolute values), b) UW value corresponds to the weaker side of peripheral vestibular function, c) DP refers to the fastest nystagmus direction elicited by caloric testing, d) in cases where bilateral weakness is observed, UW and DP will not be calculated and FI will not be considered valid, e) normal FI values should be observed in UW. (4)

X. Conclusions

The caloric test should be undertaken last, after the oculomotor motility and the positional tests have been performed. Water irrigation elicits a stronger and a faster caloric response than air irrigation. VOG is more convenient than EOG, at least in terms of calibration. The ABBT completion should be sought, unless the examinee is unable to undergo the four irrigations. In such a case, the ABBT may turn to MCST, that is, why warm caloric irrigations should be performed first. FI should be carried out for any of two irrigations (one for right beating nystagmus and one for left beating nystagmus) of the same temperature. Mean peak spvs, UW, DP and FI should be calculated. DP has little clinical significance. BS and spontaneous nystagmus denote the same anomaly. GA normative values are rather arbitrary because very few studies address this issue. In case of no caloric response, the IWCT should be performed to assess any residual low-frequency function of each horizontal semicircular canal.

Caloric testing is used to confirm that vertigo is of peripheral vestibular etiology. Caloric testing alone can not exclude dizziness of central etiology. We should bear in mind that in up to 25% of cases, it failed to aid clinical doctors to draw any conclusions. A normal caloric testing does not mean a typical vestibular function. It is reported that up to 35% of patients suffering from dizziness of peripheral vestibular etiology will have normal caloric test findings.

References

1. Baloh RW, Honrubia V. Clinical neurophysiology of the vestibular system. 2nd edition Philadelphia: FA Davis; 1990.

2. Barber HO, Stockwell CW. Manual of electronystagmography. St. Louis: Mosby; 1980.

3. N.T. SHEPHARD AND G.P. JACOBSON. The caloric irrigation test. Handbook of Clinical Neurotology, Vol. 137 (3rd series).

4. British Society of Audiology. The Caloric Test. Recommended procedure. Date of publication: April 2010.

5. SANJAY A. BHANSALI, MD, and VICENTE HONRUBIA, MD. Current status of electronystagmography testing. Otolaryngol Head Neck Surg 1999;120:419-26.

6. Internet, Electronystagmography. Wikipedia; 5 August 2019.

7. Timothy C. Hain. Vestibular testing. Internet; November 4, 2004.

8. Sanjay A. Bhansali and Vicente Honrubia. Current status of electronystagmography testing. Otolaryngology-Head and Neck Surgery; March 1999.

9. Von Gierke HE, Barber H, Cohen B et al. Working group on evaluation of test for vestibular function (CHABA). Aviat Space Environ Med 1992;63(2 Suppl):A1-34.

10. Amanda Smith, AuD; Douglas L. Beck, Aud; Michelle Petrak, PhD; Cammy Bahner, MS. In the Trenches, Part 2: Using VNG in tandem with traditional vestibular/balance tests. Hearing Review, 2012.

11. Internet, Vestibulo-ocular reflex. Wikipedia; 7 October 2019.

12. Internet, Vestibulo-Ocular Reflex – an overview. ScienceDirect Topics.

13. Purves D, Augustine GJ et al. The Otolith Organs: The Utricle and Sacculus. Neuroscience. 2nd edition. Sunderland (MA):Sinauer Associates; 2001.

14. Gary P. Jacobson, Ph.D. and Craig W. Newman, Ph.D. Background and Technique of Caloric Testing. Chapter 8. Handbook of Balance Function Testing.

15. Maxime Armstrong, MSc. The Vestibulo-ocular Reflex. Canadian Audiologist VOL. 6 – ISSUE 5 – 2019.

16. Baloh RW, Solingen L, Sills AW, et al. Caloric testing. 1. Effect of different conditions of ocular fixation. Ann Otol Rhinol Laryngol 1977;86(Suppl 43):1-6.

17. Hood JD, Korres S. Vestibular suppression in peripheral and central vestibular disorders. Brain 1979; 102:785-804.

18. Fornby C, Robinson DA. Measurement of vestibular ocular reflex (VOR) time constants with a caloric step stimulus. Journal of Vestibular Research 10 (2000) 25-39.

19. Formby C, Kuntz LA, Rivera-Taylor IM, Rivera-Mraz N, Weesner DR, Butler-young NE, Ahlers AE. Measurement, analysis and modeling of the caloric response. Evaluation of mental

alerting tasks for measurement of caloric-induced nystagmus. Acta Otolaryngol 1992:Suppl 498, 19-29.

20. Internet. Interacoustics caloric irrigation. Videonystagmography guide. March 2017.

21. Mulch G, Petermann W. Influence of age on results of vestibular function tests. Ann Otol Rhinol Laryngol 1979; 56:1-17.

22. Bruner A, Norris TW. Age related changes in caloric nystagmus. Acta Otolaryngol (Suppl) 1979; 282:1-17.

23. Karlsen EA, Hassanein RM, Goetzinger CP. The effects of age, sex, hearing loss and water temperature on caloric nystagmus. Laryngoscope 1981; 91:620-627.

24. Coats AC, Smith SY. Body position and the intensity of caloric nystagmus. Acta Otolaryngol 1967; 63:515-532.

25. Kenneth H. Brookler, M.D. The simultaneous binaural bithermal: a caloric test utilizing electronystagmography. The Laryngoscope; May 5, 1975.

26. Kenneth H. Brookler, M.D. Simultaneous bilateral bithermal caloric stimulation in electronystagmography. Laryngoscope 1976;81(7);1014-19.

27. Joseph M.R. Furman, M.D., Ph.D. Simultaneous Caloric Testing. ICS medical. ENG Report, January 1989.

28. Guy Lightfoot, Fiona Barker, Keri Belcher, Vicki Kennedy, Greg Nassar, and Frances Tweedy. The Derivation of Optimum Criteria for Use in the Monothermal Caloric Screening Test. Ear & Hearing, Vol. 30, No. 1, 54-62.

29. Fluur E, Mendel L. Habituation, efference and vestibular interplay. Acta Otolaryngol 1962; 55:65-80.

30. Torok N. Nystagmus frequency versus slow phase velocity in rotatory and caloric nystagmus. Ann Otol Rhinol Laryngol 1969; 78:625-639.

31. Kumar A. Post caloric nystagmus: an analysis of culmination frequency and maximum slow phase velocity. Acta Otolaryngol Suppl. 1995;520 Pt 1:220-4.

32. Kamran Barin, PhD. Calculating Slow Phase Velocity of Nystagmus. Audioloyonline; September 13, 2004.

33. Kamran Barin, PhD. Common Errors in ENG/VNG. Audiologyonline; July 17, 2006.

34. Internet, Caloric reflex test. Wikipedia 2 October 2018.

35. Lightfoot GR. The origin of order effects in the results of the bi-thermal caloric test. Int J Audiol 2004; 43:276-282.

36. Proctor L, Hansen D, Rentea R. Corneoretinal potential variations. Significance in electronystagmography. Arch Otolaryngol 1980; 106:262-265.

37. Cammy Bahner, MS; Michelle Petrak, PhD; Douglas L. Beck, Aud; and Amanda Smith, AuD. In the Trenches, Part 3: Caloric and Rotational Chair Tests. Hearing Review, 2013.

38. Timothy C. Hain. Caloric test (practice). Internet; February 5, 2014.

39. Kamran Barin, Ph.D. Baseline Shift and Gain Asymmetry in the Caloric Test. Insights in practice for clinical audiology, March 2010.

40. Charles W. Stockwell, Ph.D. Directional Preponderance. ICS medical. ENG Report, August 1987.

41. Raymond van de Berg, Mark van Tilburg, Herman Kingma. Bilateral Vestibular Hypofunction: Challenges in Establishing the Diagnosis in Adults. ORL 2015;77:197-218.

42. Timothy C. Hain, Marcello Cherchi, and Dario Andres Yacovinco. Bilateral Vestibular Weakness. Frontiers in Neurology; 31 May, 2018.

43. Motohisa Ikeda, Isamu Watanabe. Evaluation of Hyperactive Caloric Responses in Patients with Inner Ear Diseases. ORL 1997;59:326-331.

44. Kamran Barin, PhD. Bilateral Hyperactive Caloric Responses. Audiologyonline; December 13, 2004.

45. Denise Utscb Goncalves, Lilian Felipe, Tania Mara Assis Lima. Interpretation and use of caloric testing. Rev Bras Otorhinolaringol 2008;74(3):440-6.

46. Kamran Barin, PhD. The Fixation Suppression Test in ENG Evaluation. Audiologyonline; April 9, 2007.

47. Meredith E. Adams, MD, Steven A. Telian, MD, Robert L. Kane, MD, and Mary Butler, PhD, MBA. Monothermal Caloric Screening Test Accuracy: A Systematic Review. Otolaryngology-Head and Neck Surgery 2016, Vol. 154(6) 982-996.

48. Salatoff RT, Pavlick ML, McCaffrey JD, Davis JM, Stewart SM. Simultaneous Binaural Bithermal Caloric Testing: Clinical Value. Ear Nose Throat J. 2017 Jan;96(1):29-31.

49. Kelly A. Murphy, Arayamparambil C. Anilkumar. Caloric Testing. StatPearls – NCBI Bookshelf; February 22, 2019.

50. Internet. Indications for Caloric Testing. Neurology tests 2014.

51. Timothy C. Hain, MD. Caloric test (AKA ENG, VENG). Chicago Dizziness and Hearing; July 4, 2017.

52. Madalina Gabriela Georgesku. Hearing and Vestibular Testing in Meniere's Disease. IntechOpen; October 4th 2017.

53. Woo Seok Kang, Sang Hun Lee, Chan Joo Yang, Joong Ho Ahn, Jong Woo Chung and Hong Ju Park. Vestibular Function Tests for Vestibular Migraine: Clinical Implication of Video Head Impulse and Caloric Tests. Frontiers in Neurology; September 2016, volume 7, article 166.

54. Ognyan I. Kolev, MD, PhD and Michaela Sergeeva, MD, PhD. Vestibular disorders following different types of head and neck trauma. Functional Neurology 2016; 31(2): 75-80.