WHAT BÁRÁNY’S CALORIC TEST MIGHT HAVE OVERLOOKED: THE PRIMARY FACTOR MAY BE THE MIDDLE EAR MUSCLES

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Abstract

The caloric test of vestibular function, originating from Bárány in the early 1900s, has conventionally been understood as a test of the effect of temperature on the horizontal semicircular canals of the inner ear. Warm water introduced into the external auditory meatus will, if the vestibular system is intact, cause back-and-forth beating of the eyes (nystagmus) in one direction; cold water will cause beating in the reverse direction. The text-book explanation is that the eye movements are caused by a thermal gradient across the horizontal canal, which in turn causes convection in the fluid within. The convective motion stimulates the vestibular hair cells, causing nystagmus, dizziness, nausea, and often vomiting. But here an alternative mechanism is proposed: warm or cold water causes the tensor tympani muscle in the middle ear to increase in tension (warm water) or decrease in tension (cold water), and in this way changes the force exerted by the ossicles on the inner ear fluids behind the oval window. Altered force on the stapes therefore means a change of hydraulic pressure inside the sealed labyrinth, and this pressure could directly stimulate hair cells within the inner ear – including the semicircular canals – and so generate nystagmus. If correct, this means the caloric test is really a test of the temperature sensitivity of the middle ear muscles, although the vestibular system still needs to be intact in order to register a positive response. The new hypothesis explains a range of anomalies surrounding the caloric test, and these are systematically reviewed.

Key words: tensor tympani • temperature • muscle tension • T-jump • intralabyrinthine pressure

LO QUE SE HA PASADO POR ALTO EN LA PRUEBA CALÓRICA DE BÁRÁNY: LA EXPLICACIÓN ESTÁ EN LOS MÚSCULOS DEL OÍDO MEDIO

Resumen

La prueba calórica de la función vestibular, descrita por primera vez por Bárány a principios del siglo XX, se consideró formalmente como una prueba de la influencia de la temperatura en los canales semicirculares horizontales del oído interno. El agua caliente introducida en el canal auditivo externo causa, si el sistema vestibular está intacto, la pulsación del ojo hacia atrás y hacia delante (nistagmo) en una dirección; el agua fría causa una pulsación en la dirección opuesta. La explicación clásica es que los movimientos oculares son causados por el gradiente térmico del canal horizontal, lo que, a su vez, provoca convección y movimiento de fluidos en él. El movimiento estimula las células auditivas vestibulares, causando nistagmo, mareos, náuseas y a menudo vómitos. En este trabajo se analiza la base fisiológica de la prueba calórica y se identifica un mecanismo alternativo: el agua caliente o fría aumenta la tensión del músculo tensor del tímpano en el oído medio (agua caliente) o disminuye la tensión (agua fría) y, por lo tanto, cambia la fuerza ejercida sobre el fluido por los huesecillos detrás de la ventana oval. La fuerza alterada significa un cambio de presión en el laberinto cerrado, y es esta presión la que estimula directamente las células auditivas del oído interno – incluyendo los canales semicirculares – causando así el nistagmo. Si esta interpretación es correcta, significa que la prueba calórica es en realidad una prueba de la sensibilidad a la temperatura de los músculos del oído medio, aunque, por supuesto, las células sensoriales del sistema vestibular deben estar intactas para dar una respuesta positiva a los cambios de presión. La nueva hipótesis explica una serie de anomalías asociadas a la prueba calórica, que se verifican sistemáticamente.

Palabras clave: tensor del tímpano • temperatura • tensión muscular • presión intralabiríntica

ЧТО УПУЩЕНО В КАЛОРИЧЕСКОЙ ПРОБЕ БАРАНИ? ОТВЕТ СЛЕДУЕТ ИСКАТЬ В МЫШЦАХ СРЕДНЕГО УХА

Аннотация

Калорическая проба вестибулярной функции, впервые описанная Барани в начале XX века, обычно понималась как тест влияния температуры на горизонтальный полуокруженный канал внутреннего уха. Теплая вода, введенная в наружный слуховой проход, если вестибулярный аппарат не поврежден, будет вызывать колебательные движения глаз (нистагм) назад и вперед в одном направлении; холодная вода вызовет колебательные движения в обратном направлении. Классическое объяснение
Introduction

In 1914 Robert Bárány won the Nobel Prize in Physiology or Medicine for his work on the theory and clinical application of the caloric response: when warm or cold water is introduced into a patient’s ear canal, they experience strong vestibular symptoms – their eyes begin flickering (nystagmus) and they become dizzy, often leading to severe vomiting [1–4]. Although the response had been documented for many years earlier, Bárány was the first to develop it into a useful clinical tool [5–7]. He also provided an appealing theoretical model to explain how it worked.

The response is still clinically important, for it indicates whether or not the semicircular canals responsible for balance are functioning normally [8,9]. Usefully, it can point to which canal – left or right – is dysfunctional (or weak) based on how strongly each ear responds to irrigation. Other vestibular tests (which stimulate bilaterally) are unable to make this distinction. Although in modern times the caloric test has become less common – it is unpleasant and takes much clinical time – it is still the gold standard for assessing balance problems [10]. Nowadays the vHIT test (the video Head Impulse Test) is more often employed because it is quicker, easier, and better tolerated, even though it cannot determine the side of weakness [11,12].

Bárány explained his findings in terms of circulation cells set up by a thermal gradient in the horizontal canal (the semicircular canal closest to the outer ear), likening endolymph in the canal to water heated by a hot stove [1,3,7]. In both cases, warming of the fluid causes it to expand and rise, producing a circulation cell, and it is this fluid motion that supposedly stimulates the horizontal canal and produces nystagmus (Figure 1). As Figure 1A shows, the horizontal canal is fairly close to the ear canal and almost projects into the middle ear space. His hypothesis explains why the nystagmus reverses, beating in the opposite direction, when cold water is used instead of warm or when the patient is placed in an inverted posture. It also explains why the beating of the eyes is from left to right – in the horizontal plane – since the horizontal canal responds to rotations in this plane.

Figure 2 summarises the outcomes when the beating is measured for all body angles and for both warm and cold water. The symmetrical curves suggest that Bárány’s simple model broadly accounts for the clinical findings.

However, over the intervening years a number of anomalies have arisen with the caloric test. Together, these have not been enough to overturn the underlying theory, since certain secondary effects can be invoked, but they have certainly made it unclear how the caloric effect is produced [3,12,14]. Here, a review is made of a diverse range of evidence, and a new hypothesis put forward which appears to avoid the anomalies: simply put, the proposal is that the caloric response arises from the effect of temperature on the middle ear muscles. It is well known that when any muscle is warmed, its power increases, and when cooled,
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it weakens [15]. Applied to the middle ear muscles – the tensor tympani in particular – this means that the force exerted on the stapes will either increase or reduce, and these changes will cause an increase or reduction in pressure of the labyrinthine fluids [16]. In the end, it is this change in fluid pressure which disturbs the equilibrium of the hair cells in the semicircular canal and causes nystagmus.

A connection between inner ear pressure and vestibular effects has already been described [16,18,19], so it follows that warming or cooling of the ear canal could in this way produce pronounced vestibular reactions. This paper explores the connections and sets out evidence supporting the proposed middle ear muscle mechanism.

The following text sets out various anomalies surrounding the existing theory, after which the proposed mechanism involving the tensor tympani muscle is described more fully. Just as with any isometric muscle, cold water will reduce its tension and warm water will increase it. In turn, the altered tension will cause a corresponding adjustment in the force exerted on the stapes and on the fluid-filled labyrinth behind it, altering the internal hydraulic pressure. As will be shown, this proposed mechanism overcomes the anomalies associated with Bárány’s explanation, and predicts other distinct outcomes consistent with the literature.

In summary, the locus of action for both the old and new models is the horizontal canal, but there is an important intermediary which to date has been ignored: the tensor tympani muscle. It is this muscle which reacts to temperature and produces pressure changes in the canal – which in turn produce vestibular effects. The text provides an anatomical and physiological journey through the middle ear and semicircular canals, and shows how involvement of the tensor tympani opens up a new perspective on how the labyrinth functions.

Anomalies in the caloric response

The caloric response works in zero gravity

Perhaps the strongest and most direct evidence against the convection current idea is that the caloric response persists in zero gravity, when buoyancy forces are absent. And yet, when two astronauts aboard the 1983 Spacelab mission were tested while in orbit, they experienced nystagmus with an intensity comparable to when they were on the ground [3,20–22]. Since convective currents rely on gravity to create buoyancy, the persistence of the caloric response under weightless conditions directly contradicts the Bárány model.

A somewhat different, but related, set of experiments have been done with 20 subjects who were tested during the weightless phase of flight – only about 10 seconds long – when an aircraft performs a parabolic trajectory [23]. Interestingly, for three-quarters of the trials, the nystagmus reversed direction during the weightless phase, although it did disappear entirely in the other quarter. The persistence of nystagmus under microgravity provides more evidence against the convective cell idea.
Experiments with subjects in a centrifuge are of interest because, although no weightless condition can be produced, the g-forces can be closely manipulated for extended periods [24]. It has been found that the slow phase velocity of the nystagmus – the rate at which the eyes drift (in degrees per second) before rapidly flicking back – is directly proportional to the g-force, at least in the range 1–1.8 g. Extrapolation back to zero-g then corresponds to about zero slow phase velocity, which can be taken as an indication that, at least for one subject, Bárany’s notion might be broadly correct.

At this point it is also worth noting the results of work done on monkeys in which their semicircular canals were surgically plugged [25]. In this case, the caloric responses persisted undiminished.

Scientifically, then, it is evident that there is much more going on with the caloric test than just temperature-induced buoyancy. Nevertheless, the idea that thermal gradients are responsible for the observed nystagmus has almost universally prevailed [4,10]. To account for persistence under zero-g, some have proposed that temperature causes a direct expansion of the endolymph in the canal, and hence deflection of the cupula [3, 22, 26], or thermal effects on the neural structures themselves [14,20].

One idea with merit is that the semicircular canals are intimately connected to the otolithic organs, so that when g-forces change the gravity sensors in the utricle or saccule, perhaps by some piezoelectric sensing mechanism, then their output modulates the rotation sensors of the semicircular canals [20]. Scherer and Clarke calculate that only 10–20% of the caloric response can be attributed to gravity, and that 80–90% is due to displacement of fluid volumes, perhaps by thermal expansion. We will return to this modulation idea later on, where it will be suggested that it is the static pressure exerted by the middle ear muscles on the whole labyrinth which provides the modulating signal.

However, despite its noted inadequacies, the Bárany mechanism continues to be the core model presented in the literature [4,8–9,27–28].

**Disjunct between the caloric and vHIT tests**

Another drawback of the Bárany model is inconsistency with the other standard vestibular test, the video head impulse test (vHIT). The test was devised a decade or more ago and involves monitoring a subject’s eye movements with a camera located inside a set of goggles while the head is given a sudden jerk in the plane of the horizontal canal [11]. The speed of the eyes’ response, mediated by the vestibulo-ocular reflex (the eye muscles are aligned in the same plane as the semicircular canals), gives a measure of how well the horizontal canals are functioning. Since the jerk affects both canals, it is not possible to conclusively say which canal is impaired. Nevertheless, the test is quick, easy, and not unpleasant, so it has superseded the caloric test in most clinics.

The interesting point, however, is that the results of the caloric and vHIT tests often disagree, even though they are both supposed to be testing the integrity of the semicircular canals [11]. There are various degrees of dissociation. For example, Rambold [12] tested 1063 hospital patients and while 24% failed the caloric test, only 5% failed the vHIT test. In like manner, Stahle [3] noted that a caloric response can be elicited from “dead ears” – that is, ears in patients who, during or after a rotation test, show no nystagmus, indicating apparent insensitivity of the horizontal canal. Such nystagmus is called “paradoxical” because nystagmus is still elicited by warm and cold water. However, the most clear-cut separation between the two tests is seen in Meniere’s patients, who may have greatly reduced or absent semicircular canal function as indicated by the caloric test, but have normal canals as shown by the vHIT test [11,29–30].

Various explanations have been offered in the literature for the divergent outcomes. A common one is to suppose that each test measures different response frequencies: about 0.003 Hz in the case of the caloric response (because it takes minutes for the thermal effects to act) compared to about 2.5 Hz for the vHIT stimulus (acting over half a second). One might suppose, for example, that one frequency band might be detected by ‘Type 1 hair cells and the other by Type 2. However, this distinction seems physically unrealistic, recognizing that reaction to a stimulus frequency less than one-hundredth of a cycle per second is rather unlikely. Rambold [12] says there is unlikely to be such a division of frequencies because no response is discernible when a rotary chair is moved at 0.003 Hz. McGarvie and colleagues [29–30] attempted to explain the dissociation found in Meniere’s cases in terms of expansion of the membranous labyrinth from endolymphatic hydrops. They supposed that convection in the semicircular canal was less effective when the endolymph cross-section expanded. Another possible explanation, however, is that Meniere’s disease is not due to hydrops at all but to dysfunction (cramp or dystonia) of the middle ear muscles [18]. Under this interpretation, it is the affected muscles of Meniere’s patients which are less able to respond briskly to temperature. The issue is taken up again in a later section.

**The thermal stimulus is minuscule**

The complications just noted bring us to a list of other processes that have been called on as candidates for generating nystagmus in response to water irrigation. Consider the anatomy of the situation, as illustrated in Figure 3. It is clear that when warm or cold water is placed in the ear canal, the first structure to experience a change in temperature will be the tympanic membrane (left of Fig. 3). Of course, the bone surrounding the ear canal will also begin to rise in temperature, but it has relatively high thermal inertia, and it will take some time for heat to be conducted through the temporal bone and reach the semicircular canals some distance away (right of Fig. 3). According to O’Neill [14], the temporal bone is a highly insulating medium for heat transfer and his experiments on a series of temporal bones showed that heat was only slowly conducted along them. He points to the related observations of Harrington [6], who found that when the bony ridge between the external ear canal and the semicircular canal was removed, it had little effect on measured temperatures. Both O’Neill and Harrington conclude that heat must somehow be conducted across the middle ear space (see also [31–33]).
At the same time, one should note that the caloric response occurs within the first 10–20 seconds of irrigation, while the effects of a standard 7-degree temperature offset persist for many minutes [8–9]. When air stimulation is used (necessary in space), the stimulation temperature can be rapidly changed, and Baumgarten and colleagues [35] report that nystagmus reverses direction within a few seconds. And yet the associated temperature change at the horizontal semicircular canal appears to be only a small fraction of a degree [2,6,14,17,36,37], making it difficult to see how such small stimuli could have appreciable and lasting physiological effects. This is especially so when the effective stimulus is supposed to be a circulation cell set up in a narrow tube by a temperature gradient (see Figure 1). It is even more remarkable when one notes that nystagmus can be induced using water only 0.1°C above or below body temperature [38].

In contrast to the long and diffuse conduction pathway through the temporal bone, it is significant that the eardrum is in intimate contact with the malleus (mass of just 30 mg), which is in turn directly connected to the tensor tympani (Figure 3). This paper makes the case that it is this pathway which is involved in producing the caloric response. A rise (or fall) in the temperature of the eardrum is quickly conveyed to the malleus and the tensor tympani, and this then causes tensing or relaxation of the muscle. As described by Bell [16,18], the tensor tympani directly controls the hydrostatic pressure within the labyrinth, so warming it will lead to an increase in force (and pressure) and cooling it will lead to a reduction in force and pressure.

More details are presented later, but in overview, warming produces an increase in pressure, manifested as a beating of the eyes to the left, and cooling produces a reduction in pressure, resulting in beating of the eyes to the right – in accord with clinical observations.

A revealing anatomical cross-section is shown in Figure 4, which well illustrates the difference in the two possible conduction pathways. Figure 4 (from [14]) is based on the projected image of a temporal bone slice and it shows the short conduction pathway (and low thermal inertia) of the route to the tensor tympani and the longer distance and higher thermal inertia of the path to the horizontal semicircular canal.

To provide wider perspective, many modelling efforts have been made to study thermal conduction through the temporal bone and the effect on the semicircular canal [14,22,28,39–44]. There is not the space to go into detail, but it is of interest to note that a number of them claim, implicitly or explicitly, to confirm the Bárány model. The basis is often that, given enough time and a sufficiently sensitive vestibular apparatus, eventually some temperature rise will be detected, even if only a fraction of a degree. Such a rise in temperature is not disputed; the real issue is whether such a small rise is physiologically effective. Patki et al. [45] surveyed various thermal conduction studies over the decades and raised the question of whether canal temperature can in fact be regarded as a true marker of the observed vestibular responses. The same group [10] investigated correlations between anatomical dimensions extracted from CT scans and caloric response parameters, but the correlations were weak – a multivariate model required almost as many parameters (nine) as subjects (eleven) to provide a fit, suggesting something crucial may have been missed.

The proposition put forward here is that the temperature changes reaching the tensor tympani are quicker and greater than those which eventually reach the semicircular canals – and that the pressure change induced in the labyrinth by the tensor tympani could be the key parameter.
**Other anomalies**

A number of other anomalies arise from the convection theory, although not all of them are dealt with here. Instead, the reader is referred to Longridge et al. [46] where these additional problems are discussed and references given. The Longridge work is also useful in listing different possible explanations, based on Jongkees [47], that have historically been put forward to explain the caloric response. All of them appear to encounter major objections, while none of them identify a role for the middle ear muscles.

The main problems that Longridge and Jongkees raise with existing theories are the following.

1) Given the 3D anatomical arrangement of the three canals, the angle at which the patient is tilted in order to give zero response (i.e., when the horizontal canal should be exactly horizontal) is at about 285° body tilt, not 300° as expected (see Fig. 2). In a similar way, the other point of zero response is at an angle of 140°, not 120° as expected. That means that the difference between the two zero points is only 145°, not 180° as consideration of the gravity vector would imply.

2) The convection theory speaks of convection currents of endolymph in a semicircular canal only 0.3 mm in diameter, a physically unlikely situation. In addition, the canal contains two distinct compartments, one filled with endolymph and the other with perilymph, with the boundary being a very thin membrane separating the endolymph of the membranous labyrinth from the outer bony labyrinth. Longridge notes that complex modelling has been done on endolymph movements, but the contribution of perilymph has not yet been carefully assessed. The only consideration of perilymph dynamics seems to be in the model of Iversen and Rabbit [42] where cupula fluid displacements at 0.003 Hz are calculated, but no attention is given to static perilymph pressure.

3) It is inconsistent with the convection picture that the responses are larger when the subject is on their back (face up) than when they are face down, and larger in response to cold water than to warm. These features are also evident in Figure 2.

4) Finally, and perhaps most convincingly, there is the anomaly that when the semicircular canals suffer damage and are nonfunctional, a normal caloric reaction can sometimes still be demonstrated. A summary of this work, undertaken by a range of researchers over several decades, is given in Jongkees [47], and the rest of this section considers this important aspect in more detail.

Jongkees notes, as an example related to him by Passe, that patients with Meniere’s disease who have undergone “electrocoagulation” of the horizontal canal (in an effort to ameliorate their condition) still exhibit a normal caloric response, even though this canal is now completely non-functional. Similarly, in Jongkees’ own work, he reports it is not uncommon to find a “paradoxical” caloric reaction in which there is a negative rotatory test (indicating that the semicircular canals are not functioning as they should) but still a positive caloric test (warm and cold water still produce nystagmus). Strengthening the paradox, there is earlier evidence from Borries who reports that when pigeons had the membranous portion of their semicircular canals surgically removed, the animals still remained responsive to the caloric test [48]. Significantly, when the birds were turned upside down, the nystagmus reversed direction, replicating the same feature as seen in normal humans when they are inverted. Borries concludes that the caloric nystagmus does not originate from the crista, but from the remaining otolith organs, and Jongkees sees the force of this conclusion, although in 1948 he was unable to reconcile it with his own views on the matter, confirming his review with the comment that “many facts remain which cannot be explained by the theory of Bárány.”

In Jongkees’ opinion, the caloric reactions are probably a response of the entire labyrinth, including the otolithic organs. He thinks the organs might react to the thermal stimulus – perhaps even by raising or lowering intralabyrinthine pressure (a vascular mechanism suggested by van Caneghem in the mid-twentieth century), after which the otolithic organs react and trigger nystagmus. Although unlikely, the theory does entertain the possibility that intralabyrinthine pressure could have an effect.

It would appear that the ensuing years have not resolved anomalies like these, and indeed the introduction of the vHIT test appears to have compounded them. Curthoys and Manzari [11] are encouraged that the vHIT test helps in understanding semicircular canal function, but the fact is that the test does not dispel the puzzle of why the caloric test shows normal horizontal canal function in patients with vestibular complaints.

Before moving on, let us briefly examine Jongkees’ idea that the balance system is an integrated unit which involves interactions between the semicircular canals and the nearby otolithic organs. Conventionally, it is thought that the semicircular canals are responsible for detection of head rotation, while the otolithic organs are responsible for detection of gravity and linear acceleration [13, 49]. However, a number of researchers have identified interactions [20], and indeed the approach has much to recommend it. An interaction helps one understand how a change in static pressure (as produced by the middle ear muscles) might be sensed by the otolithic organs and then used to modulate the semicircular canals (and produce nystagmus). This paper supports the modulation idea, and puts it forward as the reason for the sine-wave-like curve in Fig. 2. Pressure and the gravity vector combine to produce a force on the otolithic organs, and this resultant modulates the semicircular canal output. Of course, not only is the gravity vector changed when the body is tilted through various angles, intracranial pressure is changed as well, and this factor will also have an effect in modulating slow wave velocity.

The modulation idea helps provide a fuller picture of what is going on with the caloric response, but in many ways it is supplementary to the middle ear muscle theory and so only the core of the concept is sketched here (beginning near the bottom of p. 15). The main concern of this paper is to describe the middle ear muscle mechanism and set out evidence supporting it.
A new model of the caloric response

The basic mechanism behind the caloric response can be simply stated: all skeletal muscles undergo an increase in their tension when they are warmed and a decrease in tension when cooled [15,50,51]. Applied to the tensor tympani, this means that temperature will cause an increase or decrease of pressure inside the labyrinth. Figure 3 shows the anatomical arrangement, and it can be appreciated that when the tensor tympani increases or decreases its force, the stapes will change its position in the oval window and cause a corresponding increase or decrease in the pressure of the fluids behind it. This mechanism is essentially the same as that by which the middle ear muscles protect the cochlea from overload – by contracting and increasing pressure on hair cells (the intralabyrinthine pressure theory [16]) – except on a slower timescale. As will be shown, the middle ear muscle mechanism appears to explain the facts surrounding the caloric response and avoid the anomalies outlined previously.

Muscles and temperature

It is well known that mammalian skeletal muscles are particularly sensitive to temperature: when any such muscle is cooled its resting tension decreases; conversely, when warmed, its tension increases [50,52]. As well as being widely employed in sports medicine, this “potentiation” is key to the theory of the caloric response set out here. The effect involves active cross-linking processes between the muscle filaments in which temperature changes their tension. The model gives a good description of the change in tension of an isometric muscle when it is subject to a sudden jump in temperature (a T-jump) – the situation encountered during a caloric test.

For brevity, the extensive literature on the detailed physiology and biochemistry of T-jumps will not be given. The interested reader is referred to Hill [15]; Ranatunga et al. [54]; Coupland and Ranatunga [50]; and their references. The basic point is that all mammalian striated muscles react in a similar way to temperature changes. In mammals, the response to a T-jump is almost sigmoidal, with tension steadily increasing when temperature rises and decreasing when temperature falls (Fig. 3 of [53]). Significantly, the sigmoidal response means that at higher temperatures the tension begins to level off.

Applied to the middle ear muscles, which operate isometrically, the cross-bridge model gives a good description of the caloric test: warming will increase tension (and hence pressure in the labyrinth); cooling produces the reverse. These changes in pressure will be reflected in changes in the slow phase velocity of nystagmus, giving the responses shown in Figure 2.

The sigmoidal response of muscle to temperature means that nystagmus will be more sensitive to cooling than to warming, and this is just what we see in Fig. 2. Based on the data of [17], the plot shows that, for five subjects, the average slow phase velocity peaks at –23 deg/s for cold irrigation but reaches only +13 deg/s for warm irrigation (both stimuli differ by 7°C from body temperature). This result supports the middle ear muscle model.

The new model gives an account of how changes in the resting tension of the tensor tympani translate directly to altered pressure in the fluids filling the labyrinth. To understand this relationship, one needs to appreciate the intralabyrinthine pressure (ILP) theory of middle ear muscle function, a theory that was commonplace in otolaryngology a century ago but which gradually fell out of favour. Reasons for why the ILP theory deserves renewed attention are set out in (16), and further implications are discussed in [18,19,55].

Recapitulating these ideas, the ILP theory points to the special anatomical arrangement of the tensor tympani by which contraction of the muscle pulls the whole ossicular chain inwards, towards the oval window. Incidentally, the name ‘tensor tympani’ comes from the fact that the tympanum becomes visibly tensed when the muscle contracts [56] – see Figure 3. Contraction therefore pushes the stapes into the oval window, raising the pressure of the fluids behind it. Because endolymph and perilymph are incompressible and are confined within the solid bone of the labyrinth (the only point of pressure relief is the elasticity of the round window membrane), the pressure inevitably acts on all the sensing cells inside the labyrinth. One set of cells is the outer hair cells of the cochlea; another is the hair cells of the otoliths and semicircular canals. A fundamental aspect of the ILP theory is that the sensing cells respond to and are regulated by the static pressure that surrounds them. In brief, pressure in the labyrinth squeezes the hair cells and adjusts their resting sensitivity. The result is that the firing rate of the cells is regulated by contraction of the middle ear muscles; indeed, the raison d’etre of these muscles is to regulate the neural gain of the whole inner ear system.

For the cochlea, it means that the sensitivity of all the thousands of hair cells can be rapidly and simultaneously controlled with a delicate muscle contraction. For the balance organs the implications are less clear, but one consequence is that if the pressure undergoes an inadvertent change – such as by a sudden cooling or warming of the middle ear muscles – the resulting disturbance manifests as nystagmus. Warming will increase tension and pressure, so nystagmus will beat to the left; cooling on the other hand will ease tension and pressure, so nystagmus will beat to the right.

Modulation effects: an auxiliary model

A potentially helpful synthesis of a diverse literature is to see that the key parameter driving nystagmus is the difference between the pressures in the left and right labyrinths. This difference drives the slow phase velocity, and so explains why the slow phase velocity can be negative or positive depending on which labyrinth experiences the greater pressure. This idea can be incorporated into a modulation model in the following way.

A recurring finding in the literature is that the outputs of the semicircular canals and of the otolithic organs affect
each other [20, 46]. This is reasonable given that both form part of an integrated system. The most direct form of the idea is that the output of the otolithic organs modulates the output of the semicircular canals [20], and it is worthwhile briefly setting out this auxiliary hypothesis – for it explains many of the observations concerning the caloric response, in particular the sine-wave-like modulation of slow phase velocity as seen in Figure 2. That is, the gravity receptors in the saccule and utricle respond to the gravity vector as the body is tilted through 360°, and it is this signal which modulates the nystagmus.

Scherer and Clarke [20] build a gating mechanism which largely explains the changes in the caloric responses with body tilt as found by Coats and Smith [17]. The refinement made here is that it is the static pressure generated by the middle ear muscles which modulates the system, with pressure supplementing the gravitational forces to which the otolithic organs respond. The caloric test, then, can have an immediate effect on the otolithic organs, which in turn modulate the semicircular canals. This explains why cyclic g-forces generated during up-and-down parabolic flight (zero to 2 g) directly modulate the slow phase velocity of nystagmus (Fig. 1 of [23]). The extra refinement is that it is the difference in pressure between the left and right inner ears that drives the nystagmus signal. Thus, when both ears are irrigated simultaneously, only a small response is observed [38,57]. In the same way, when one ear is stimulated by a loud sound, a fixation target will appear to move in one direction or the other, but when both ears are stimulated, no motion is seen [58], an observation that can be understood in terms of the middle ear muscles and their acoustic reflex (which again generates pressure in the labyrinth).

Bance and colleagues proposed [59] that the nystagmus generator acts on the differential input between the two sides; they also assumed that this signal is then compared to a floating reference which aims to minimise the nystagmus. In this way, it becomes possible to understand why the baseline of the slow wave velocity is often offset from zero (and sometimes different in each ear) – there is a bias or directional preponderance so that the resting pressure is different to that in the other. It also accounts for why in the later stages of a caloric test the slow wave velocity can often go negative [9,23].

Evidence supporting the model

This section summarises how the middle ear muscle model explains the anomalies pointed out earlier. Later, attention is drawn to otherwise puzzling evidence which supports the model.

First, then, it is possible to understand why the caloric test works in space: the thermal stimulus does not drive convection currents, as Bárány thought, but instead affects the temperature of the middle ear muscles, leading to static pressure adjustments; in turn, the response of pressure-sensitive cells in the otolithic organs then triggers nystagmus.

Second, a disjunct between the caloric and vHIT tests is naturally to be expected since the latter is probing the response of the semicircular canals to rotation, whereas the former is testing the temperature sensitivity of the middle ear muscles (together with secondary responses of the otolithic system to hydraulic pressure). A similar consideration explains the "paradoxical" caloric reaction in which the nonfunctioning of the semicircular canals does not mean that nystagmus cannot be generated – for the middle ear muscles are still able to generate pressure disturbances when their temperature is altered, and the otolithic organs can still respond to the pressure and trigger nystagmus.

The earlier anomaly concerning the unrealistically small magnitude of thermal stimuli reaching the labyrinth is overcome by recognising the high sensitivity of muscle to temperature, and the close proximity of the middle ear muscles to the eardrum and ossicles. As pointed out, there is a direct thermal pathway from the ear canal to the muscles. Moreover, it is known that the entire balance system is exquisitely sensitive to alterations in static pressure [60].

Next, it can be appreciated how, if the otolithic organs simply modulate the output of the semicircular canals, then the main features shown in the two curves of Fig. 2 need not be perfectly symmetrical. The pressure in the labyrinth is at least a combination of cerebrospinal fluid pressure (which, via the cochlear aqueduct, equilibrates with the inner ear pressure) and middle ear muscle induced pressure, so the zero points need not be 180° apart. Of course, consideration of the how muscles are more susceptible to cold than warm stimulation, discussed earlier, explains the greater response to cold water than warm.

Evidence directly implicating the middle ear muscles

Before the introduction of antibiotics, radical mastoidectomy was a common surgery for severe middle ear infection [61]. It meant that the entire middle ear was resected, including the ossicles and their attachments. The operation created a severe hearing deficit in the affected ear as well as eliminating any middle ear muscle function. Significantly, another side-effect of radical mastoidectomy – as reported by McKenzie [62] for all 6 of his cases – was that the operated patients exhibited no, or minimal, response to caloric irrigation. At the same time, they still had functioning labyrinths, with all cases complaining of fluctuating vertigo (which was treated with surgical destruction or drugs). The strong implication is that a vigorous caloric response requires an intact middle ear muscle system. Since true radical mastoidectomy is now rare – with "modified" radical mastoidectomy (Bondy’s procedure) seeking to preserve the middle ear structures – further investigation is needed to substantiate the role of the middle ear muscles. (Tending to confuse the issue, modified radical mastoidectomy is often just called radical mastoidectomy in the recent literature.)

Jongkees (1948) summarises a report from Hennebert in 1946 who noted that brushing the temple, and similar manual stimulations, caused an easing of nystagmus and the fading of spinning sensations induced by a caloric test. In this context it should be noted that applying a touch to the face is a standard way of stimulating the tensor tympani, which is innervated by the facial nerve [63–65]. Jongkees himself was able to confirm this finding, observing how the nystagmus would disappear upon touch, although
deviation of the eyes remained and the total time-span of the caloric response was unaffected (as might be expected from cooling or warming the muscle). He also relates a much earlier finding from 1918 in which Kobrak was able to amplify the caloric response by applying pressure to the tragus, another likely stimulus to the tensor tympani. Jongkees also describes experiments in which strong, sustained caloric stimulation eventually affected the cochlea, so that sounds appeared distorted (double hearing or diplacusis) – a result also pointing to involvement of the middle ear muscles [56,66]. In addition, he describes how Thielemann in 1924 was able to halt the caloric reaction by applying a local anesthetic (cocaine) to the middle ear mucosa, a treatment expected to disable the middle ear muscles. Finally, a later paper by Jongkees [38] describes how rubbing the cheek with alcohol changes the frequency of nystagmus, and how a completely silent room or closing the eyes tightly disturbs the caloric response – all situations that point to reflex involvement of the middle ear muscles.

Also worth noting is a study of subjects with hyperactive acoustic reflexes, a condition in which there are unusually strong and sensitive middle ear muscles [67]. Intriguingly, one such subject had, in addition, a hyperactive vestibular response on caloric stimulation (p. 404 [3]).

Meniere’s disease

Meniere’s disease is a puzzling entity, and there is still no agreed explanation in the literature [68]. However, one recent proposal is that a Meniere’s attack is due to a sudden cramp or dystonia of the middle ear muscles [18], although more research is needed to confirm the speculation. Nevertheless, if the middle ear muscle theory of Meniere’s disease is correct, and that middle ear muscles are in fact involved in caloric responses, then we should expect to see Meniere’s disease sufferers with abnormal caloric responses – since the common factor is impaired middle ear muscle function. Indeed that is the case, with the general finding being that patients with Meniere’s disease have healthy head impulse test results but abnormal caloric results ([11], p. 10 [49]); see also [69–72].

Park et al. [70] studied 38 Meniere’s patients, and found that less than half (42%) had unilateral weakness on the caloric test, but even among these, most of them (10 of 16 = 63%) had substantially normal head-thrust tests. The authors conclude that subjects who are still suffering Meniere’s attacks have largely preserved canal function. As an outstanding example, one subject who had 100% unilateral weakness under the caloric test still showed nystagmus from irrigation of the affected ear (albeit with some asymmetry), indicating that canal function was still largely intact.

McGarvie and colleagues [29,30] assessed the dissociation between caloric tests and head impulse tests in 22 Meniere’s patients and found that the caloric test indicated that the affected ear had an average weakness (or canal paresis) of 66% compared to the unaffected ear, even though the vHIT test indicated that the Meniere’s group had VOR (vestibulo-ocular reflex) gains indistinguishable from a matched set of healthy ears. They concluded that the standard explanation – loss of hair cells in the horizontal canal – is unlikely to be correct because the group usually had normal vHIT responses. Instead, the authors suggest that the disjunct might be explained in terms of Meniere’s patients having an enlarged endolymphatic cross-section in the membranous labyrinth, but as pointed out before this mechanism is physically unlikely. On the other hand, the involvement of the middle ear muscles has the virtue of explaining both the origin of Meniere’s disease and, in affected individuals, why their caloric responses might often be compromised (because of dysfunction of their middle ear muscles) while their vestibular responses remain largely unaffected (because there is nothing substantially wrong with their semicircular canals).

This picture is also a reasonable explanation for the similar disjunctions found by Lee et al. [71] who were inclined to fall back on the “endolymphatic expansion” theory (and reliance on different neural responses at 0.002 Hz and at 2–3 Hz) even though this differential seems physiologically unlikely [12]. Moreover, the authors acknowledge that the expansion theory fails to explain other Meniere’s symptoms like migraine, and conclude by supposing there must be another mechanism at play (p. 706 [71]). Finally, we note that tenotomy – cutting of the tendons of the middle ear muscles – has been shown to be a particularly effective treatment for Meniere’s disease [73–75].

Pressure as a vestibular stimulus

The model above regards raised intralabyrinthine pressure, created by the middle ear muscles, as an effective stimulus to the inner ear. Specifically, it views changes in temperature of the muscles – produced by ear canal irrigation – as giving rise to vestibular effects, notably nystagmus. This is consistent with the general connection evident in the literature between hydrostatic pressure in the labyrinth and vestibular dysfunction, and in this section the aim is to make this connection more explicit.

A notable paper in this context is an experimental study by Baumgarten and colleagues [76] who found a remarkable equivalence between changing hydrostatic pressure in the labyrinth and caloric stimulation. Motivated by the results obtained from astronauts in zero-g – which clearly indicate that some “nonthermoconvective” mechanism is required – Baumgarten and colleagues performed experiments on pigeons and discovered that the effects of increasing or decreasing hydrostatic pressure in the labyrinth were indistinguishable from warming or cooling of the horizontal semicircular canal. Increase of pressure always caused nystagmus in the same way as that observed during warm stimulation, and decrease of pressure mimicked nystagmus from cold irrigation. Moreover, inversion of the pigeon caused inversion of the pressure-induced nystagmus, an effect in line with the body tilt experiments of Coats and Smith (Figure 2). In other words, no convection hypothesis is required, just pressure and the effect of posture, which Baumgarten and colleagues ascribed to a modulating action of the otoliths.

The equivalence between pressure change and caloric stimuli can of course be generalised to say that in the ear canals of humans it is the pressure change alone – generated by the tensor tympani – which causes nystagmus.
The pressure effects noted by the German group are also of interest in shedding light on another curious phenomenon in otology known as alternobaric or pressure vertigo [77]. Alternobaric vertigo is of concern to scuba divers and pilots because a rapid change in pressure in can under certain conditions lead to a sudden spinning sensation and loss of orientation. The complaint is usually caused by a difference in middle ear pressure between one side and the other, perhaps from a blocked Eustachian tube. For divers, however, there is a double danger: pressure vertigo and caloric vertigo. Both are brought on by unbalanced ear stimulation, from either failing to equilibrate pressure in both ears or by letting cold water trickle into one ear only (www.diversalertnetwork.org/health/ears/vertigo). The point to be noted is that vertigo induced by a pressure imbalance is equivalent to that caused by cold water. The equivalence, of course, is not coincidence: the basic thesis of this paper is that caloric vertigo is in fact pressure vertigo induced by reaction of the middle ear muscles to a change in temperature.

Experiments with alternobaric vertigo in the laboratory offer additional support. Ingelstedi and colleagues [77] were able to induce vertigo in a number of normal subjects by placing them in a sealed chamber and altering the chamber pressure over some tens of seconds, a procedure that produced changes in middle ear pressure (so long as the subjects kept their Eustachian tubes closed). The experimenters found that they could induce pressure vertigo (as seen by horizontal nystagmus) in 5 of 79 subjects; these subjects had an asymmetry in the pressure at which each of their Eustachian tubes were forced open. The threshold of nystagmus was reached when the pressure difference between the ears was about 20–50 cm of water (2–5 kPa). Significantly, the recorded nystagmus was to the right when the right ear pressure exceeded that in the left, and was directed to the left in the reverse situation, which is again a nice analogy to the warm and cold caloric tests and consistent with the results of the Baumgarten group.

The general perspective is that vestibular effects can arise from any action which (asymmetrically) raises inner ear pressure: raised cerebrospinal fluid pressure [78–79], increased ear canal pressure (Hennebert’s sign), Valsalva manoeuvre [77], or body tilt [80–81]. Simple changes in posture – from head up to head down, for example – lead to pressure changes in the labyrinth, producing measurable changes in tympanic membrane position and acoustic thresholds [81]). More recent work with otoacoustic emissions confirms that body tilt has a definite effect on the cochlea [80,82–87], and also presumably on the rest of the inner ear, since all the fluids within the bony labyrinth must be at the same hydraulic pressure.

Similarly, vestibular effects can also arise from stimulation of the middle ear muscles [88–90]. Such associations have a natural explanation in terms of the intralabyrinthine pressure theory [16,18] which directly links activation of the middle ear muscles with raised intralabyrinthine pressure. In humans, the Tullio reaction is well known (vestibular reactions due to loud sounds) and its clinical effects have been linked to changes in inner ear pressure [88,91–92]. It is notable that the Tullio effect is seen even in deaf individuals [91,93], implying that sound is having a direct physical effect on the balance organs, not via any neural interaction.

Given the picture of middle ear muscles controlling intralabyrinthine pressure, this raises another interesting question concerning vestibular evoked muscle potentials (VEMPs), which are electrical responses of muscles in the neck or eye to very loud sounds, and have traditionally been seen as a direct neural reaction of the saccule to loud sound [94]. VEMPs have been used in diagnosing Meniere’s disease [72,95]. Although the saccule may be directly sensitive to sound, another possibility is that the VEMP reaction is a neural response to the increase in intralabyrinthine pressure created by contraction of the middle ear muscles, placing it in the same category as the Tullio phenomenon and the Hennebert reaction.

How does pressure produce vestibular effects?

First it should be remarked that very small increases in static pressure – fractions of a centimeter of water (less than 0.1 kPa) – are sufficient to induce vertigo-like symptoms in animal models [96] and produce measurable potassium currents in isolated Type 2 vestibular hair cells [60].

Rabbitt [28] gives a general survey of vestibular functions and disorders, including nystagmus-like reactions induced by posture, temperature (the caloric test), and sound (Tullio effect), and aims to bring them together by identifying a common locus. The structure of most interest, of course, is the cupula in the semicircular canal (Figure 5),

Image: Figure 5. The cupula is a gel which sits on top of the hair cells and spans the complete width of the membranous labyrinth. Any lateral displacement of endolymph in the semicircular canal therefore generates differential pressure and deflects the cupula sideways (black arrow). However, it is also found that the nerve bundle responds to static pressure (red arrows) which is identical on both sides of the cupula. This latter response means the cupula could respond to changes in fluid pressure produced by the middle ear muscles when caloric stimuli are applied. Adapted from [28] (CC-BY 4.0)
and Rabbitt proceeds to explain the caloric response in terms of the standard buoyancy model (Fig. 6 of [28]). Supported by previous finite-element modelling, Rabbitt and colleagues have identified differential endolymphatic pressure across the cupula – that is, its displacement – as the effective stimulus to this sensor.

However, the point to be emphasised is that there must be more to the story than just transcupular pressure. Rabbitt and colleagues have also performed experiments on the semicircular canals of the toadfish and have observed – unexpectedly – that its cupula is also sensitive to what they call “dilatational pressure”, that is pressure which is common to both sides of the cupula (red arrows in Fig. 5). The significance here is that common-mode pressure could also arise in the labyrinth from any action of the middle ear muscles which increased or decreased static pressure – such as from caloric stimulation.

According to the modelling of Rabbitt and colleagues, the dilatational pressure stimulates the cupula through distention of surrounding ampulla and consequent deformation of this delicate gel, possibly by a micrometer or less. The theoretical calculations of Oman and Young [97] suggest a threshold displacement of only 10 nm (or angular deflection of 0.001°) in response to a pressure difference across the cupula of just 10 μPa. Perhaps such vanishingly small displacements are physically detectable, but a more likely mechanism, given the findings of direct stimulation of vestibular hair cells by hydrostatic pressure, is that the hair cells themselves are intrinsically pressure-sensitive [60]. The experiments by Düwel and colleagues found that isolated hair cells had pressure thresholds of about 100 Pa; however, it is supposed that an intact cupula would have a very much higher sensitivity. A general proposal for how hair cells can act as pressure sensors has been made [98–99].

Yet Rabbitt and colleagues do not view the cupula as capable of physiologically reacting to static pressure in the labyrinth. They point to how their common mode pressures were generated dynamically by compressing the semicircular canal on both sides of the cupula at rates above 0.4 Hz, and they only measured pressures relative to perilymph (not absolute values, which would be needed in order to examine the role that combined canal pressure plays in exciting hair cells). Moreover, they note that semicircular canal afferents did not respond when the experimenters manipulated perilymph pressure, although this might have been because the set-up was not physiological (the bony labyrinth was open to the air in order to provide experimental access).

The question is therefore left open to further investigation. Nevertheless, despite the methodological limitations, the findings of Rabbitt and colleagues are suggestive, and, together with related findings, encourage the view that the labyrinth is a structure sensitive to static pressure.

Adding to the strength of that view is the work of Kondrachuk and colleagues whose modelling directly supports the idea that the cupulo-endolymphatic system is sensitive to very small changes in intralabyrinthine pressure [100]. Their modelling indicates that only very small changes in compressibilities in the system (as small as $2 \times 10^{-7}$) would be sufficient to produce a neural response to 50 mPa of dilatational pressure.

The other consideration to keep in mind is that the static pressures involved may be having an appreciable effect on the nearby otolith organs – the utricle and saccule – whose role is to detect minute changes in gravitational forces. Given the neural connections between the otolithic organs and the semicircular canals, and the potential for one to modulate the other (as outlined on pp. 15–16), then static pressures such as produced by the middle ear muscles might be having a direct effect on the otolithic organs. This possibility is enhanced by observing the anatomical make-up of these organs in which the gel layer on top of the hair cells contains a well-formed cavity – perhaps compressible – adjacent to each hair cell bundle (e.g., Fig. 1 of [101]).

**General discussion**

The essence of the above text is to make the case that the trigger for the caloric response is in the middle ear muscles, not the semicircular canals. As with all muscles, these dynamic structures are sensitive to temperature (as well to vibration [55] and cramp [18]). So when warm or cold water is introduced into the ear canal the tensor tympani reacts by increasing or decreasing its tension, and this is directly transmitted to the stapes, where it is converted to pressure in the labyrinth. The tensor tympani is directly connected to the malleus which in turn is in intimate contact with the eardrum. The result is that irrigation water quickly cools or warms the ear drum and very soon after the tensor tympani (see Figs 3 and 4).

This thermal/mechanical route is much more effective than the slow thermal pathway through the temporal bone. Ultimately, it is the static pressure in the labyrinth that gives rise to the observed vestibular effects, not buoyancy. Nevertheless, it could turn out that pressure and temperature are each effective vestibular stimuli whose relative effectiveness still needs to be determined. Scheerer and Clarke [20], for example, suggested that 10–20% of the caloric response was due to what they ascribed to gravity, with the rest due to temperature. Reassessment of these percentages, in the light of the pressure effects suggested here, appears to be in order.

The new explanation avoids the multiple anomalies associated with the original convection model of Bárány, and these have been individually addressed above. Over the years, various refinements of the convection model have been proposed in efforts to fix its problems, but none of them appear to be physically realistic or overcome the identified objections. Despite persistent efforts over a century, it would seem that neither conduction, convection, or radiation [31] nor buoyancy or endolymph expansion [27] are able to adequately explain the caloric response. Against this backdrop, there are three strong pieces of evidence in favour of the middle ear muscle model: i) the caloric response works in zero gravity; ii) radical mastoidectomy eliminates the caloric response; and iii) the caloric response persists when the horizontal semicircular canal has been destroyed.
The new model is amenable to experimental test, and one convincing test might involve tenotomy: if the tendon to the tensor tympani were cut, this would interrupt the thermal conduction pathway and the caloric response would disappear. Another simple and powerful test would be to measure the frequency of spontaneous otoacoustic emissions (SOAEs) while conducting a caloric test in the opposite ear. There are strong indications that SOAE frequencies are a function of intralabyrinthine pressure \([83,85]\), and Bell has estimated that the frequency shift is about 20 Hz/kPa, a parameter that might be useful as a noninvasive measure of intralabyrinthine pressure \([16]\). Since the middle ear muscles are part of a bilateral system, one test of the new model would be to monitor SOAE frequencies over the course of a caloric test.

**Conclusion**

It is easy to gain the impression that the Bárány theory has persisted, despite its anomalies, because there has been nothing better to take its place. A confounding factor is that the stimulus identified here (temperature acting on the middle ear muscles) is accompanied by another parallel stimulus (flow of heat to the semicircular canals), so isolating them is difficult \([45]\). As a result, experiments on dead specimens continue to show temperature changes, even if they are small and slow \([17,31]\). The true stimulus to the labyrinth, this paper suggests, might be muscle-imposed pressure, not direct heat flux to the balance organ.

The problem is compounded by a general lack of attention to the middle ear muscles and of their role in regulating inner ear function. Moreover, there has been little work done on how vestibular function is affected by pressure, largely because a suitable way of measuring intralabyrinthine pressure still awaits development. This paper highlights the pivotal role the muscles have in regulating intralabyrinthine pressure, and clarifying this function is an area for further research. Longridge and colleagues \([46]\) noted the "poor understanding" we have of how the caloric response works, and Jongkees \([47]\) expressed the view that an "extratubular influence" was undeniable. Although it is now more than a century since the caloric test was first established clinically, it appears there is much more work that still needs to be done.

The caloric test is now less commonly used, but perhaps it is time to revisit many of its intriguing aspects and gain new insights into the connections between hearing and balance. The middle ear muscles are silent guardians of the inner ear, and the caloric test appears to bring out the crucial role they play in protecting and regulating that hidden organ.

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