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VESTIBOLOGY

The role of vestibular cold caloric tests in the presence of spontaneous nystagmus

Il ruolo del test monotermico freddo in presenza di nistagmo spontaneo

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SUMMARY

Objective. The bithermal caloric test is commonly used to detect a canal paresis. However, in case of spontaneous nystagmus, this procedure can provide results of non-univocal interpretation. On the other hand, confirming the presence of a unilateral vestibular deficit can help to differentiate between central and a peripheral vestibular involvement.

Methods. We studied 78 patients suffering from acute vertigo and showing spontaneous horizontal unidirectional nystagmus. All patients were submitted to bithermal caloric tests, and the results were compared with those obtained using a monothermal (cold) caloric test.

Results. We demonstrate the congruence between the bithermal and monothermal (cold) caloric test through mathematical analysis of the results of both tests in patients with acute vertigo and spontaneous nystagmus.

Conclusions. We propose to perform the caloric test in the presence of a spontaneous nystagmus using a monothermal cold assuming that the prevalence of the response to the cold irrigation on the side towards which the nystagmus beats is a sign of the presence of pathological unilateral weakness and therefore more likely peripheral in its origin.

KEY WORDS: vestibular caloric test, acute vertigo, canal paresis, directional preponderance, spontaneous nystagmus

RIASSUNTO

Obiettivo. *Il test calorico bitermico è comunemente usato per rilevare una riduzione dell'attività di un singolo labirinto. Tuttavia, in caso di nistagmo spontaneo, questa procedura potrebbe fornire risultati di non univoca interpretazione. D'altra parte, la conferma della presenza di un deficit vestibolare unilaterale potrebbe aiutare a differenziare tra un coinvolgimento vestibolare centrale e uno periferico.*

Metodi. *Abbiamo studiato 78 pazienti affetti da vertigine acuta e che mostravano un nistagmo spontaneo orizzontale unidirezionale. Tutti i pazienti sono stati sottoposti al test calorico bitermico, i cui risultati sono stati confrontati con quelli ottenuti attraverso un test calorico monotermico freddo (ice water test).*

Risultati. *Attraverso un'analisi matematica dei risultati di entrambi i test in una serie consecutiva di pazienti con vertigine acuta e nistagmo spontaneo, la congruenza tra il test calorico bitermico e quello monotermico freddo può essere dimostrata.*

Conclusioni. *Si propone di eseguire il test calorico in presenza di un nistagmo spontaneo, utilizzando uno stimolo monotermico freddo, considerando che la prevalenza della risposta alla prova fredda sul lato verso cui batte il nistagmo sia indicativo della presenza di deficit labirintico monolaterale.*

PAROLE CHIAVE: *test calorico, vertigine acuta, preponderanza direzionale, preponderanza labirintica, nistagmo spontaneo*

Introduction

The bithermal caloric test is most suitable for identifying unilateral lesions of the peripheral vestibular system as it allows the independent evaluation of each ear. The standard caloric stimulus is performed by irrigating the external

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ear canal with 250 mL of water for 30 seconds. The water temperature is 30°C for cool irrigation and 44°C for warm irrigation. Abnormal responses are recorded as canal paresis or directional preponderance [1]. However, when a spontaneous nystagmus is present, this procedure may yield results of non-univocal interpretation while simultaneously exposing the patient to an unpleasant sensation. The availability of a one-temperature caloric test would shorten the time required to complete vestibular function assessment while mitigating any discomfort experienced by the patient during caloric testing. Moreover, confirming the presence of a unilateral vestibular deficit may help to differentiate between a central and a peripheral vestibular involvement. Acute peripheral vertigo (APV) is one of the most common causes of peripheral vestibular involvement [2], accounting for 2.5% of emergency healthcare visits [3]. Nevertheless, focal cerebellar stroke, especially in the posterior-inferior cerebellar artery (PICA) area of vascularisation, may mimic APV, with acute vertigo being the only presenting symptom [4,5], the so-called pseudo-APV [6]. Between 5 and 25% of isolated dizziness may be related to a posterior fossa infarction [3,6,7], with a reported initial misdiagnosis rate of up to 28% [8].

The HINTS examination (Head Impulse test, Nystagmus, Test of Skew) is now widely recommended to diagnose acute vestibular syndrome (AVS) of central origin and differentiate it from more common peripheral vestibular diseases. When properly performed, clinical examination based on HINTS is more sensitive in identifying small posterior circulation strokes causing isolated acute vertigo than early diffusion-weighted MRI imaging [9]. In order to train emergency physicians to correctly diagnose a central cause of AVS, other protocols have been proposed: the STANDING (SponTAneous, Nystagmus Direction, head Impulse Test) in 2014 [10], the TiTrATE paradigm (timing, triggers and targeted bedside examination) [11] and, more recently, the ATTEST approach (associated symptoms, timing and triggers, examination signs and testing) [12]. None of the proposed protocols or algorithms for the evaluation of AVS have included caloric testing, although a unilateral weakness to caloric stimuli could significantly impact differential diagnosis [13]. On the other hand, in the presence of spontaneous nystagmus, classic bithermal tests may be difficult to interpret and may not be recommended [13,14]. The main purpose of this study is to evaluate the possibility of detecting a pathological unilateral weakness in the presence of spontaneous nystagmus using only a caloric cold test (ice water test) [15] and to recommend the use of this procedure in the differential diagnosis of APV from central nervous system (CNS) diseases that may present as an isolated vertigo.

Materials and methods

A cohort of 78 patients was considered (41 males and 37 females; ages ranging from 20 to 88 years, mean 55 years), all suffering from acute vertigo and presenting a spontaneous horizontal unidirectional nystagmus. All patients underwent bithermal caloric tests using the Fitzgerald-Hallpike technique. The external auditory canal was separately irrigated with 125 ml of warm (44°C) and cold (30°C) water in a 30-second period, with a 7-min interval between the two tests. Responses were recorded by an infrared eye-tracking system (GN Otometrics, Taastrup, Denmark), which is able to automatically extract both the mean frequency and the mean Slow Phase Velocity (SPV) of the thermally induced nystagmus. In accordance with Jongkees' formulae, the software then calculates the degree of Canal Paresis (CP) based on both frequency (freqCP) and SPV (spvCP). According to the authors' experience, CP values > 25% can be considered pathological (pathological CP), while values between 15% and 25% may be potentially significant (borderline CP). The Jongkees' formulae were used to obtain the values of canal paresis and directional preponderance: the congruence with the results obtained algebraically can also be verified experimentally. The cold caloric test was performed as follows: while the patient was lying in the supine position with the head inclined by 30°, the patient's head was rotated to the left side (90°) and the external ear canal was irrigated with 2-3 ml of cold water (melted with three ice cubes in order to maintain water temperature between 1 and 3°C) [16]. After 30 seconds, the patient straightens the head and following an additional 30 seconds the vestibular response was assessed (in terms of frequency, total number of nystagmus beats, and angular velocity of the slow phase in the stiffness phase) (Fig. 1). After 10 minutes, the test was repeated on the contralateral side.

Results

In 36 patients, the spontaneous nystagmus was directed rightwards, while in 42 patients it was directed leftwards. A total of 63 patients received a diagnosis of Acute Unilateral Vestibulopathy (AUV), while 4 were diagnosed with Menière's Disease. In 8 patients, acute vertigo was a consequence of a central vestibular involvement: 6 cases of vertebro-basilar insufficiency (4 of these patients showed signs of white matter lesions on MRI), one case of Wallemberg syndrome and one patient suffering from systemic vasculitis with CNS involvement. Finally, 3 patients were diagnosed with vestibular migraine. The results of the bithermal caloric test and ice water test are reported in Table I. In all cases, the cold caloric test provided coherent results with the values of canal paresis and directional prepon-

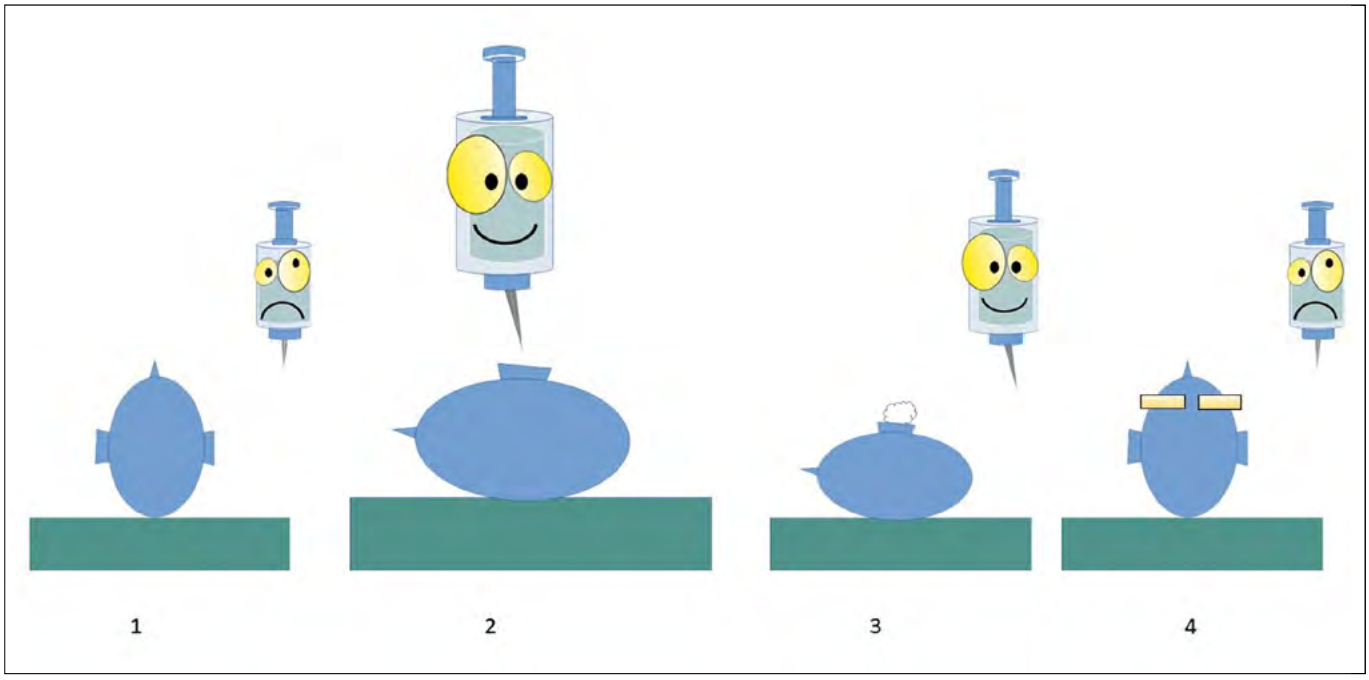

Figure 1. Monoaural cold test. 1-2) the patient is instructed to lie in the semi-recumbent position with the head tilted forward 30 degrees; 3) approximately 2 ml of ice water is injected into the ear canal via syringe and kept in that position for 30 seconds; 4) the patient's head is then turned midline and observed for nystagmus while the patient performs alerting tasks. After 5 minutes, the test is repeated on the contralateral side.

derance and brisker responses than bithermal tests: if the spontaneous nystagmus was directed to the right side and the cold test had produced a greater response on the right ear than the left, then canal paresis exceeded directional preponderance (being therefore pathological), making the spontaneous nystagmus more likely to be peripheral. In all cases, the directional preponderance was congruent with the spontaneous nystagmus (positive if the spontaneous nystagmus was directed to the right and negative if the spontaneous nystagmus was directed to the left). The congruence with the results obtained algebraically has also been verified experimentally.

With the above-described procedure, two values could be obtained:

- the response of cold stimulation on the right (*rc*); and
- the response of cold stimulation on the left (*lc*).

These results can be used to assess the presence of a pathological canal paresis (CP).

Demonstration

Premise:

$$uw = \frac{(rw + rc) - (lw + lc)}{rw + rc + lw + lc} * 100$$

$$dp = \frac{(rw + lc) - (lw + rc)}{rw + rc + lw + lc} * 100$$

(With the condition $rw + rc + lw + lc \neq 0$); *uw* unilateral weakness, *dp* directional preponderance, *rw* right warm, *lw* left warm, *rc* right cold, *lc* left cold).

If the caloric nystagmus beats towards the opposite direction (it goes to the right instead of the left or vice versa), it is represented with a negative sign.

In this example, a spontaneous nystagmus directed to the right is considered.

Demonstration

Working hypotheses:

Hypothesis 1)

$dp \neq 0$, because if there is a spontaneous nystagmus it is assumed that there is also a pathological directional preponderance; therefore $(rw + lc) - (lw + rc) \neq 0$ (the numerator of the formula for *dp* is non-zero); *dp* must also be positive in the hypothesis that the nystagmus beats to the right.

Hypothesis 2)

- $rw > 0$ (warm stimulation of the right ear cannot reasonably inhibit or reverse nystagmus if it is directed rightwards);
- $lc > 0$ (cold stimulation of the left ear cannot reasonably inhibit or reverse nystagmus if it is directed rightwards).

Consequently, $rw + lc > 0$ (the sum of two positive numbers is positive).

Table I. The results of monothermal cold tests and the values of Canal Paresis (CP) and Directional Preponderance (DP) evaluated with bithermal caloric test. The last two columns highlight the fact that there is always agreement between the cold test that gives the greatest response and the values of CP and DP: if the spontaneous nystagmus beats to the right and the cold right test gives a greater response than the cold left, then there is certainly a canal paresis greater than the directional preponderance (therefore pathological) making spontaneous nystagmus more likely to be peripheral. In all cases, DP was congruent with the spontaneous nystagmus (positive if the spontaneous nystagmus was directed to the right and negative if the spontaneous nystagmus was directed to the left). Note cases 36 and 78 in which, the cold tests being symmetrical, the labyrinthine preponderance was equal to the directional preponderance.

	Age	Gender	Diagnosis	RC	LC	CP	DP	Congruence	
Right beating spontaneous nystagmus									
1	68	M	AUV	0	12	43.8	118.8	R < L	CP < DP
2	65	M	AUV	13	41	7.6	54.6	R < L	CP < DP
3	68	F	AUV	0	58	-6.2	83.1	R < L	CP < DP
4	64	F	VM	36	45	1.0	10.0	R < L	CP < DP
5	38	M	AUV	15	21	74.4	88.4	R < L	CP < DP
6	23	M	AUV	27	32	75.3	86.5	R < L	CP < DP
7	80	M	AUV	-9	25	118.5	244.4	R < L	CP < DP
8	63	F	AUV	5	12	84.2	121.1	R < L	CP < DP
9	37	F	AUV	0	38	108.3	266.7	R < L	CP < DP
10	38	F	AUV	0	28	100.0	240.0	R < L	CP < DP
11	84	F	AUV	0	13	100.0	188.3	R < L	CP < DP
12	47	M	AUV	22	32	58.2	80.2	R < L	CP < DP
13	65	F	AUV	0	25	90.0	215.0	R < L	CP < DP
14	52	M	AUV	0	30	25.0	100.0	R < L	CP < DP
15	61	M	AUV	0	20	100.0	197.6	R < L	CP < DP
16	59	M	AUV	0	20	4.8	68.3	R < L	CP < DP
17	24	F	AUV	-27	50	54.8	545.2	R < L	CP < DP
18	66	M	VBI	21	31	67.6	102.6	R < L	CP < DP
19	29	F	AUV	0	37	9.8	100.0	R < L	CP < DP
20	48	F	WALL	42	60	0.9	17.9	R < L	CP < DP
21	67	F	AUV	15	25	45.7	67.4	R < L	CP < DP
22	70	M	AUV	0	30	-22.2	44.4	R < L	CP < DP
23	47	F	AUV	0	40	66.7	200.0	R < L	CP < DP
24	37	F	AUV	0	25	29.6	100.0	R < L	CP < DP
25	49	F	AUV	0	20	70.7	168.3	R < L	CP < DP
26	55	F	AUV	21	26	22.9	34.9	R < L	CP < DP
27	88	F	VBI	32	38	26.2	37.9	R < L	CP < DP
28	82	F	AUV	11	12	61.9	65.1	R < L	CP < DP
29	59	F	AUV	56	20	59.7	7.9	R > L	CP > DP
30	63	M	AUV	43	18	56.0	10.1	R > L	CP > DP
31	80	M	AUV	22	13	61.2	34.3	R > L	CP > DP
32	53	F	AUV	47	45	8.0	6.1	R > L	CP > DP
33	65	M	AUV	24	18	60.0	46.6	R > L	CP > DP
34	62	F	SV	30	27	20.7	15.7	R > L	CP > DP
35	51	F	VM	22	21	15.5	13.8	R > L	CP > DP
36	54	M	AUV	47	47	10.9	10.9	R = L	CP = DP
Left beating spontaneous nystagmus									
37	68	M	AUV	53	44	-24.8	33.7	L < R	CP < DP
38	29	M	MD	50	46	-11.5	16.1	L < R	CP < DP
39	55	F	MD	47	9	22.0	54.0	L < R	CP < DP
40	63	M	AUV	30	16	-30.2	62.8	L < R	CP < DP

continues ▶

Table I. The results of monothermal cold tests and the values of Canal Paresis (CP) and Directional Preponderance (DP) evaluated with bithermal caloric test. The last two columns highlight the fact that there is always agreement between the cold test that gives the greatest response and the values of CP and DP: if the spontaneous nystagmus beats to the right and the cold right test gives a greater response than the cold left, then there is certainly a canal paresis greater than the directional preponderance (therefore pathological) making spontaneous nystagmus more likely to be peripheral. In all cases, DP was congruent with the spontaneous nystagmus (positive if the spontaneous nystagmus was directed to the right and negative if the spontaneous nystagmus was directed to the left). Note cases 36 and 78 in which, the cold tests being symmetrical, the labyrinthine preponderance was equal to the directional preponderance *(follows)*.

Left beating spontaneous nystagmus									
	Age	Gender	Diagnosis	RC	LC	CP	DP	Congruence	
41	43	M	VM	15	5	-3.6	39.3	L < R	CP < DP
42	51	F	AUV	42	0	2.4	100.0	L < R	CP < DP
43	45	F	AUV	16	11	-100.0	123.3	L < R	CP < DP
44	62	M	AUV	34	0	-19.0	100.0	L < R	CP < DP
45	46	F	MD	47	-10	35.4	79.8	L < R	CP < DP
46	67	F	AUV	36	0	-34.9	121.7	L < R	CP < DP
47	48	F	AUV	14	0	-79.5	151.3	L < R	CP < DP
48	72	M	AUV	43	0	-1.0	87.0	L < R	CP < DP
49	63	F	VBI	14	0	-17.6	100.0	L < R	CP < DP
50	59	M	AUV	30	18	106.1	142.4	L < R	CP < DP
51	52	F	AUV	25	-15	-31.7	226.8	L < R	CP < DP
52	35	F	AUV	30	0	-47.4	152.6	L < R	CP < DP
53	87	F	VBI	36	0	-5.3	100.0	L < R	CP < DP
54	48	M	AUV	15	10	-87.0	108.7	L < R	CP < DP
55	67	M	AUV	41	0	-93.3	230.0	L < R	CP < DP
56	33	M	AUV	37	0	-103.6	238.2	L < R	CP < DP
57	69	M	VBI	40	0	-7	100.0	L < R	CP < DP
58	50	M	MD	17	0	-67.2	117.9	L < R	CP < DP
59	20	F	AUV	15	12	-56.5	65.2	L < R	CP < DP
60	29	F	AUV	40	0	-72.4	210.3	L < R	CP < DP
61	40	M	AUV	36	9	-4.9	57.3	L < R	CP < DP
62	67	F	AUV	20	0	-44.4	100.0	L < R	CP < DP
63	30	F	AUV	23	27	-70.7	61.0	L > R	CP > DP
64	55	M	AUV	38	40	-22.4	20.9	L > R	CP > DP
65	71	F	AUV	18	31	-97.7	67.4	L > R	CP > DP
66	35	M	AUV	40	42	-14.8	12.4	L > R	CP > DP
67	48	M	AUV	18	28	-37.2	20.7	L > R	CP > DP
68	65	M	AUV	0	25	-100.0	7.4	L > R	CP > DP
69	47	M	AUV	28	31	-58.1	52.4	L > R	CP > DP
70	44	M	AUV	7	8	-100.0	93.3	L > R	CP > DP
71	65	M	AUV	25	31	-51.5	39.8	L > R	CP > DP
72	41	M	AUV	0	30	-187.5	62.5	L > R	CP > DP
73	72	M	VBI	6	16	-82.4	52.9	L > R	CP > DP
74	73	F	AUV	0	21	-100.0	26.3	L > R	CP > DP
75	60	M	AUV	11	17	-106.9	86.2	L > R	CP > DP
76	45	M	AUV	12	20	-77.6	45.9	L > R	CP > DP
77	62	M	AUV	38	40	-14.9	12.6	L > R	CP > DP
78	70	M	AUV	15	15	-55.2	55.2	L = R	CP = DP

RC: Right Cold test, number of the nystagmus beats at culmination; LC: Left Cold test, number of the nystagmus beats at culmination; M: male; F: female; AUV: Acute Unilateral Vestibulopathy; VM: Vestibular Migraine; Wall: Wallemberg syndrome; VBI: Vertebro-Basilar Insufficiency; SV: Systemic Vasculitis with CNS involvement; MD: Menière's disease.

Demonstration

Calculations

If the directional preponderance is strictly positive (hypothesis 1):

$$dp = \frac{(rw + lc) - (lw + rc)}{rw + lc + lw + lc} * 100 > 0$$

This is true in two cases:

a) $\begin{cases} (rw + lc) - (lw + rc) < 0 \\ rw + lw + rc + lc < 0 \end{cases}$

or:

b) $\begin{cases} (rw + lc) - (lw + rc) > 0 \\ rw + lw + rc + lc > 0 \end{cases}$

Case a)

Adding member to member (two negative numbers will generate another negative number), so:

$(rw + lc) - (lw + rc) + rw + lw + rc + lc < 0$

$rw + lc - \cancel{lw - rc} + rw + \cancel{lw + rc} + lc < 0$ *(-lw* and *+lw* cancel each other out, as *-rc* and *+rc)*

$rw + lc + rw + lc < 0$

$2 * (rw + lc) < 0$

$rw + lc < 0$ (this is not acceptable according to hypothesis 2)

Case b)

Adding member to member (two positive numbers) another positive number should result, so:

$(rw + lc) - (lw + rc) + rw + lw + rc + lc > 0$

$rw + lc - \cancel{lw - rc} + rw + \cancel{lw + rc} + lc > 0$ *(-lw* and *+lw* cancel each other out, as *-rc* and *+rc)*

$rw + lc + rw + lc > 0$

$2 * (rw + lc) > 0$

$rw + lc > 0$ (which is in accordance with hypothesis 2)

Hypothesis a) is excluded and only hypothesis b) is considered valid, which provides:

b) $\begin{cases} (rw + lc) - (lw + rc) > 0 \\ rw + lw + rc + lc > 0 \end{cases}$

If *dp* is pathological (hypothesis 1) and $uw \geq dp$, then *uw* is also pathological (normal values are of the same order of magnitude and almost the same in all laboratories) and the nystagmus is more likely of peripheral origin.

$$uw \geq dp$$

$$\frac{uw}{dp} \geq 1$$

It can be divided by *dp* first and second member of the inequality because $dp > 0$ (hypothesis 1).

We may replace the Jongkees' formulas:

$$\frac{\frac{(rw + rc) - (lw + lc)}{rw + rc + lw + lc} * 100}{\frac{(rw + lc) - (lw + rc)}{rw + rc + lw + lc} * 100} \geq 1$$

or:

$$\frac{(rw + rc) - (lw + lc)}{rw + rc + lw + lc} * \left(\frac{rw + rc + lw + lc}{(rw + lc) - (lw + rc)}\right) \geq 1$$

(both denominators are strictly positive: point b).

Simplifying:

$$\frac{(rw + rc) - (lw + lc)}{(rw + lc) - (lw + rc)} \geq 1$$

$$\frac{rw + rc - lw - lc}{rw + lc - lw - rc} - 1 \geq 0$$

$$\frac{rw + rc - lw - lc - rw - lc + lw + rc}{rw + lc - lw - rc} \geq 0$$

$$\frac{2 * (rc - lc)}{rw + lc - lw - rc} \geq 0$$

and since the denominator is positive, the numerator must also be positive (or equal to 0).

So:

$$2 * (rc - lc) \geq 0$$

$$rc - lc \geq 0$$

$$rc \geq lc$$

The mathematical steps are all reversible so that the following can be concluded.

In the case of a nystagmus directed to the right, if unilateral weakness is greater than the directional preponderance, the cold right stimulus should produce stronger responses than the cold left.

In the case of a nystagmus directed to the right, if the cold right response is brisker than the cold left, unilateral weakness predominates over directional preponderance.

The above conclusions are valid regardless of the nystagmus dimension considered [frequency and slow phase velocity (SPV)].

Discussion

The presence of a canal paresis in the acute phase of a vertiginous attack may point towards a vertigo of peripheral origin, although this finding alone is not sufficient for a complete differential diagnosis. Nevertheless, it represents an important indicator that, together with other clinical and instrumental data, may be useful in distinguishing peripheral vestibular involvement from central involvement [5].

The presence of a spontaneous nystagmus makes it difficult to perform and interpret a bithermal caloric test which is therefore generally not recommended. A recent study recommends abandoning caloric testing and replacing it with

video Head Impulse Test (vHIT) in the acute setting [14]. On the contrary, the present study may confirm the usefulness of caloric testing if performed using the simplified method (monothermal cold caloric tests), while considering that an asymmetric caloric response can also occur with central vestibular pathologies. Moreover, vHIT and other advanced pieces of equipment may not be available in all clinical settings (especially in the Emergency Room). Indeed, the application of cold caloric tests alone in most cases does allow the determination of whether a canal paresis is present, though it does not measure the percentage of its impairment (information that is not strictly necessary). The algorithm presented in Figure 2 provides an example.

1. If the cold thermal stimulation generates a greater response on the right side than the left, the spontaneous nystagmus (directed to the right) is more likely to be peripheral in origin, or, at least, a pathological labyrinthine preponderance is present. The same process can be applied in terms of sign symmetry, in the case of a left-directed nystagmus: if the left cold response is more intense than the right, a pathological labyrinthine preponderance is present.
2. If the cold right response is equal to the cold left response, then the labyrinthine preponderance is equal to the directional preponderance, and since a spontaneous nystagmus is present, the directional preponderance can be considered pathological. Therefore, the labyrinthine preponderance is also pathological, which implies that the nystagmus is more probably peripheral in origin.
3. If the right cold response is less evident than the left cold, it is only possible to say that the unilateral weakness is less relevant than the directional preponderance; however, this finding is not determinant for the differential diagnosis.

In fact:

Example 1

$uw = 30$; $dp = 40$

(There is a pathological unilateral weakness, even if less than the directional preponderance, $uw < dp$: more likely peripheral nystagmus).

Or:

Example 2

$uw = 5$; $dp = 40$

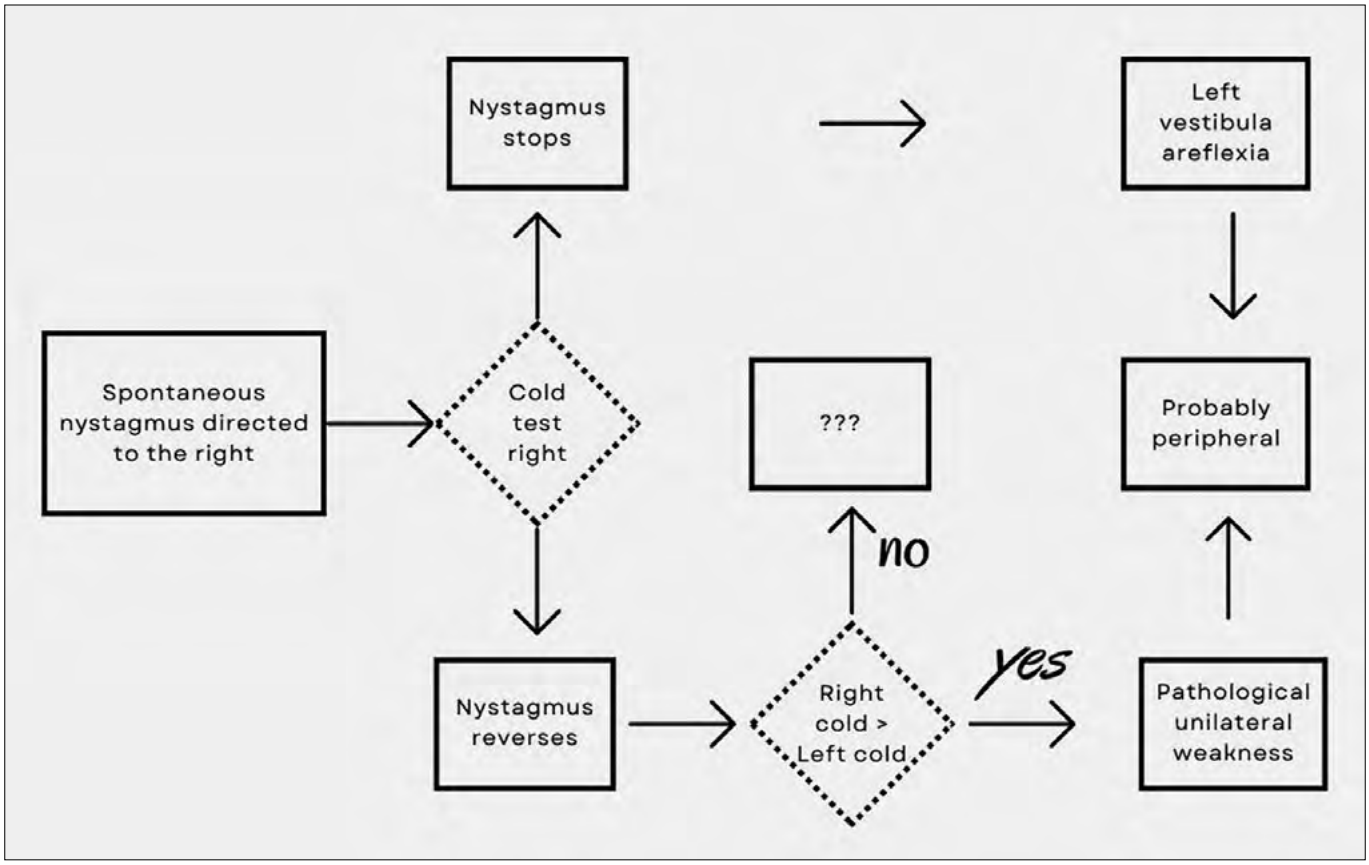

Figure 2. Algorithm for diagnosis of pathological labyrinthine preponderance with cold tests only.

(There is no pathological unilateral weakness, but *uw* < *dp*: more likely central nystagmus).
In both cases *uw* < *dp*, but the first case is more likely to be central in origin, the second case is more likely peripheral. Therefore, in the event of a right-beating nystagmus, if the right cold response is less evident than the left cold response, a spontaneous nystagmus directed to the right is to be considered at risk of centrality. In the case of partial left labyrinthine damage, a spontaneous right-directed nystagmus is generated in the first hours of the disease when a compensatory mechanism has not been established yet. In this case, by performing a right cold test:

1. the right semi-circular canal is blocked by cold inhibitory stimulation; and
2. the left semi-circular canal prevails by virtue of its residual function, thus generating a left-directed nystagmus.

While by performing a cold caloric test on the left:

1. the left semi-circular canal is blocked due to cold inhibitory stimulation; and
2. the right semi-circular canal prevails by virtue of its full functionality, generating a nystagmus beating rightwards.

Since the right ear functions better than the left ear, the response to the cold stimulus will necessarily be less intense on the right than on the left, as in the initial stages of disease labyrinthine preponderance will always be inferior to directional preponderance.
As the compensation proceeds, a nystagmus (of compensation) directed towards the affected ear (the left in this example) is generated, which will progressively decrease the difference between the two ears in terms of cold response, until the cold left response will become preponderant compared to the cold right. In other words, as the compensation proceeds, the directional preponderance tends to decrease.
The cold caloric test cannot be considered an alternative to the clinical head impulse test. In fact, the two tests explore different frequencies and are not comparable from a pathophysiological point of view: it is not uncommon for the results of bithermal caloric tests and vHITs to differ significantly in patients with AUV and in some cases of Menière's Disease [17-19]. For this reason, we propose the cold test alongside the classical HINTs tests (including HIT). Indeed, the differential diagnosis of an acute vertigo presenting with a spontaneous nystagmus is obtained by the interpretation of a wide plethora of tests, each contributing to the final clinical picture.
The ice water test can be performed simultaneously on both ears, as previously described [20]. However, in the presence of a spontaneous nystagmus, the authors of the present study do not believe that this test can provide results equivalent to the binaural cold test. The two separate cold stimuli were chosen for multiple reasons:

- to our knowledge there is no demonstration that the sum of the two separate cold stimuli is equivalent to the simultaneous cold administration;
- the execution of the classic simultaneous cold test can be difficult to perform and does not guarantee a perfect symmetry of stimulation; and
- in the case of areflexia, only one cold stimulation (of the ear towards which the nystagmus beats) is sufficient.

This study has several limitations: the frequency range over which thermal caloric stimuli affect the horizontal canal is at the low end of the physiologic range of stimulation of the semi-circular canals. For this reason, it is possible to lose low-frequency sensitivity and yet retain middle- and high-frequency function. This study comprises a consecutive series of patients with acute vertigo and spontaneous nystagmus: in order to confirm the utility of this test to exclude central vestibular damage a prospective study should be designed. Finally, not all patients were studied with the video Head Impulse Test (vHIT), which is now considered the gold standard for the evaluation of patients suffering from acute vertigo.

Conclusions

We propose the execution of the ice water test in patients with spontaneous nystagmus to confirm the presence of AUV, avoiding the long and unpleasant procedure of the bithermal caloric test. The cold caloric test is easy to perform, well tolerated (decreases the amplitude and frequency of the spontaneous nystagmus) and can be used in any working environment (Emergency Department, Outpatient Department and even at the patient's house). Furthermore, this procedure can be useful (when combined with any other clinical, HINTS, and instrumental, vHIT, protocols) to confirm the occurrence of a canal paresis, thus pointing towards a peripheral origin of the spontaneous nystagmus.

Conflict of interest statement
The authors declare no conflict of interest.

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Author contributions
MG: study concept and design, acquisition of data, analysis and interpretation of data, study supervision; APC: study concept and design, analysis, and interpretation of data, drafting of the manuscript, study supervision.

Ethical consideration

Ethical review and approval by the local Institutional Board (Comitato Etico Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy) were waived for this study. Due to its retrospective nature, it was not considered as part of a research project. Furthermore, the study does not include new invasive or experimental procedures or diagnostic protocol; all patients underwent routinely performed tests only, according to national guidelines. Informed consent was obtained from all participants and the study was performed in accordance with the Declaration of Helsinki.

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