

Migraine patients consistently show abnormal vestibular bedside tests

Pacientes enxaquecosos consistentemente apresentam testes vestibulares de beira-de-leito anormais

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ABSTRACT

Migraine and vertigo are common disorders, with lifetime prevalences of 16% and 7% respectively, and co-morbidity around 3.2%. Vestibular syndromes and dizziness occur more frequently in migraine patients. We investigated bedside clinical signs indicative of vestibular dysfunction in migraineurs. **Objective:** To test the hypothesis that vestibulo-ocular reflex, vestibulo-spinal reflex and fall risk (FR) responses as measured by 14 bedside tests are abnormal in migraineurs without vertigo, as compared with controls. **Method:** Cross-sectional study including sixty individuals – thirty migraineurs, 25 women, 19-60 y-o; and 30 gender/age healthy paired controls. **Results:** Migraineurs showed a tendency to perform worse in almost all tests, albeit only the Romberg tandem test was statistically different from controls. A combination of four abnormal tests better discriminated the two groups (93.3% specificity). **Conclusion:** Migraine patients consistently showed abnormal vestibular bedside tests when compared with controls.

Keywords: migraine, vertigo, bedside tests.

RESUMO

Enxaqueca e vertigem são desordens comuns, com prevalência de 16% e 7% respectivamente, e comorbidade em torno de 3,2%. Síndromes vestibulares e tonturas ocorrem mais frequentemente em enxaquecosos. Pesquisamos alterações vestibulares utilizando testes de beira-de-leito em enxaquecosos. **Objetivo:** Verificar se as respostas dos reflexos vestibulo-ocular, vestibulo-medular e risco de quedas medidas por 14 testes de beira-de-leito são diferentes comparando-se enxaquecosos sem vertigem, e controles. **Método:** Estudo transversal com sessenta pessoas, 30 enxaquecosos; 25 mulheres, 19-60 anos; e trinta controles saudáveis pareados por sexo e idade. **Resultados:** Houve tendência de pior desempenho entre enxaquecosos em quase todos testes, porém apenas o teste de Romberg tandem foi estatisticamente diferente dos controles. Uma combinação de quatro testes anormais discrimina os grupos com especificidade de 93,3%. **Conclusão:** O grupo de enxaquecosos mostrou consistentemente testes vestibulares de beira-de-leito anormais quando comparados a controles.

Palavras-chave: enxaqueca, vertigem, testes de beira-de-leito.

In neurological and otorhinolaryngological outpatients units migraine and vertigo are the two most common complaints¹. Vestibular syndromes, dizziness, vertiginous syndromes as benign positional paroxysmal vertigo, Ménière disease, motion sickness, cerebellar and anxiety disorders, in whom very often dizziness is present, all occur more frequently amongst migraineurs (30-50%)^{2,3,4}. It is well known that the equilibrium depends on an interplay between vestibular mechanisms, proprioception and visual inputs. Available data suggest that this circuitry could be dysfunctional in migraine. However, the issue as how, why and to which

extent vestibular changes do occur in those subjects remains highly controversial. The objective of the present study was to test the hypothesis that bedside clinical tests specifically designed to detect subtle vestibular dysfunctions are abnormal in migraine in the absence of vestibular complaints.

METHOD

In this cross sectional study, 30 (ICHD-2004, 2nd Ed. Cod:1; 1.1 and 1.2) interictal phase migraine patients, sequentially

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recruited in our unit and 30 matched healthy controls (patients partners and medical students) were blindly examined by the same researcher (ETM) after diagnosis. Inclusion and exclusion criteria were checked by well-trained neurologists with long headache expertise (PM-F and MBV). All tests⁵⁻¹⁸ (Table 1), were performed during one single session at the same hospital facility. Inclusion criteria were age between 18

and 65 years; migraine for at least 2 years with a minimum frequency of 2 attacks monthly; and at least 1 brain Magnetic Resonance (MRI) or Computerized Tomography (CT) scan within normal limits. Exclusion criteria were informed or clinically evidenced pregnancy; two or more tension-type headache episodes (ICHD-2004, 2nd Ed. Cod:2; 2.1, 2.2) in the previous week, chronic tension type headache (coded 2.3) or

Table 1. Tests for Vestibulo-ocular Reflex (VOR), Vestibulo-spinal Reflex (VSR) and fall risk (FR) used in clinical evaluation.

Clinical test	Method	Positive result
Vestibulo-Ocular Reflex		
Head Impulse Test (HIT) ⁵	Clinician, facing and holding the subject's head at arm's length, performs a passive and unpredictable head rotational movement in a high acceleration ~ 20° to either side having the subject's eyes fixed on the examiner's nose. It may also be done vertically (Figure 1A, B, C).	Corrective saccade back to the target
Head Shaking Test (HST) ⁶	Subject's wearing Frenzel goggle with the head positioned downwards by 30°. The examiner rapidly oscillate the head (2Hz) 20 times. When the movement stops the clinician observes the presence of nystagmus.	Nystagmus; more than 5 beats
Dynamic Visual Acuity (DVA) ⁷	Subject reads the lowest possible line in a ETDRS chart positioned 2 meters ahead, than the examiner manually oscillates the subject's head horizontally at 2 Hz in each direction and the subject tries to read the same line (Figure 1D, E).	Deviation of more than 2 lines above base line
Subjective Visual Vertical (SVV) ⁸	Looking inside a bucket, without any peripheral vision, the subject vertically redirect a line drawn on the inner bottom of the bucket under the subject's subjective perception. Results measured outside with a pendulum hanging over a protractor (Figure 1F, G, H).	More than 2.5° deviation from 0° to either side
Minimal Ice Test (MIT) ⁹	Subject is fitted with a Frenzel goggle and 0.2 mL iced water (1-3°C) is plunged in the ear canal with the head turned to side and bended 30° forward. After 10 sec the head is turned straight and nystagmus is observed in the computer screen. After 5 min the same procedure is performed on the other ear.	≠ between ears responses > 25% = canal paresis
Vestibulo Spinal Reflex		
Modified Clinical Test of Sensory Interaction and Balance (mCTSIB) ¹⁰	The subject stands on a firm surface with the feet slightly apart and crossed arms, first with eyes open and then with eyes closed, for 30 sec each. The same manoeuvre is repeated on a high density foam (Figure 2D).	Normal and Minimal sway: grades 1 and 2. Moderate and Severe: grades 3 and 4
Romberg Tandem Test (RTT) ¹¹	Subject stand with feet slightly apart and arms folded across the chest with eyes open for 30 seconds and then with eyes closed for 30 seconds.	Marked sway, or: move the feet, open the eyes, uncross the arms
Past Pointing Test (PPT) ¹²	The subject is instructed to extend the arms and place the index finger of one hand on the index finger of the examiner. The eyes are then closed, the arm raised above the head, then quickly returned to the perceived starting position. The procedure is repeated five times (Figure 2A, B, C).	Index drift away from the target towards the compromised side
Fukuda Test (FT) ¹³	Subject with arms extended and eyes closed, stepping in place with examiner counting for 50 steps (Figure 2E, F).	Moves more than 50 cm ahead and turns toward one side of more than 45°
Fall Risk		
Timed Up and Go (TUG) ¹⁴	Subject rises from a standard height chair with armrests, walks 3m, turns, and returns to sit in the chair. The time to complete the path is measured with a stopwatch.	More than 13.5 sec to complete the task
5 Times Sit to Stand Test (5TST) ¹⁵	Subject seated in a chair with arms crossed under chest and feet fitted on the ground. Upon request, stands up and sit down for 5 times. Time measured with a stopwatch.	More than 10 seconds to complete the task
Forward Reaching Test (FRT) ¹⁶	Subject is asked to bend the trunk and reach as far forward as possible having both feet fixed and parallel. The extent of movement is measured with a simple yardstick.	Score 15 cm or less indicate high risk for fall
Dynamic Gait Index (DGI) ¹⁷	The subject is observed during an eight-item task within a 21 feet path walking.	Score of 19 or less out of 24 points
Pull Test (PT) ¹⁸	The subject stands with the feet slightly spread apart and is pulled backward by the shoulders (one or two steps backwards allowed) (Figure 2G).	More than 2-3 steps to keep the balance or fall backward like a log

other headache listed in groups 3-4 (ICHD, 2004) according to clinical evaluation; circulatory, respiratory, orthopedic abnormalities or generalized weakness/tiredness of any nature which could influence/preclude the clinical tests; Ménière disease, vestibular neuritis, benign positional paroxysmal vertigo or phobic vertigo; spontaneous nystagmus; any sensitive, sensorineural, motor or coordination deficits; more than 150 mL coffee, 3 tea cups, or 2 soda cans intake per day for the last 2 days, or any amount of alcoholic beverages, tobacco, anti-vertiginous drugs, anti-depressive, anxiolytic antiemetic, or pain-killers more than b.i.d. use. All subjects underwent a neurootological examination including the minimal ice test (MIT)⁹. For the MIT a difference between right and left responses greater than 25% was considered as a canal paresis¹⁹. The Wilcoxon Signed Rank, the McNemar chi-square, and the Student *t* test were used for statistical comparisons; *p*-values < 0.05 were considered significant. The local Ethics Committee approved this study (Protocol:159-11).

RESULTS

Participants were mostly females (83.3%). Migraine patients were aged 19-62 (median 39.3) years and controls 22-62 (median 38.9) years. Considering all tests together there was a clear tendency for migraineurs to perform worse than controls (*p* = 0.003), except for the SVV and the FRT (Table 2). The tests involving the vestibulo-ocular reflex (VOR) assessment (Figure 1) in general did not distinguish patients from healthy controls (*p* < 0.05).

For the MIT the nystagmus duration ranged from 16 to 218 seconds in patients. The average percentage difference between R-L ears was $20.97 \pm 15.9\%$ in the patients group and $18 \pm 11.5\%$ in controls (Figure 2).

Regarding the vestibulo-spinal reflex (VSR)(Figure 3), only the RTT was statistically different between the two groups (*p* = 0.039). For the the m-CTSIB, considering only the responses graded as 3 and 4, six migraine patients (20%) and three control subjects (10%) showed abnormal responses.

The 5TSST and the PT tests were nearly statistically different (*p* = 0.074) in contrast with other Fall Risk (FR) tests.

A combination of 4 abnormal tests distinguish patients from controls with a sensitivity of 23.3% and a specificity of 93.3% (Table 3).

DISCUSSION

The present study shows that vertigo-free migraine patients, during the interictal phase, perform worse than controls in bedside clinical vestibular tests independently from vestibular complaints.

Although various techniques may be used to address the vestibular function in migraine patients with or without

vertigo²⁰⁻²⁵, data considering vestibular bedside tests in this context are scarce.

Marcelli et al.²⁶ evaluated otoneurological abnormalities in 22 migraineurs with vestibular symptoms as compared with 18 control migraineurs without vestibular symptoms. Seventy-three percent of the subjects in the first group had vestibular dysfunctions – peripheral, central or both – contrasting with 33% in the second group. The authors suggest the presence of a subclinical vestibular system involvement in the vertigo-free migraine patients.

Chronic headache causes postural instability, which could be the result of a sensory information rearrangement leading to greater vestibular system contribution paralleled by a reduced visual component in the equilibrium control²⁴. If this is true, migraineurs would be comparatively more dependent on vestibular functions for postural control, justifying the present results.

The tests we used to evaluate the VOR were not statistically different comparing the two groups. The response evoked by high accelerations (HIT) is controlled by a variety of different sensory and motor systems apart from the vestibular system. The VOR response can change within few minutes, pointing to a VOR plasticity⁷, but this is probably not sufficient to overcome the inadequate vestibular inputs and generate adequate responses. It is possible that chronic migraineurs develop the same phenomena identified in subjects with loss of vestibular function such as hidden saccades or other strategies to compensate a putative vestibular failure. Likewise, patients may increase the gain of the cervico-ocular reflex, and possibly the smooth pursuit system.

The DVA clearly tended to show worse results amongst patients although the SVV assessment was quite similar in both groups. Neck stiffness could putatively interfere with the DVA, as it has been shown that neck motility may be impaired in migraine²⁷.

MIT is a clean and quick monothermal bedside test, essentially a low-frequency stimulus caloric test that can detect vestibular impairment not apparent during higher-frequency head rotation^{28,29}. In accordance with the other tests, data also point to a vestibular instability in migraineurs, as reflected by a greater right-to-left asymmetry and a greater response spread amongst patients.

Apropos the VSR tests, Akdal et al.³⁰ carried out a balance and gait comparative study in 30 patients with vestibular migraine, 26 migraine without vertigo subjects, and 30 individuals without migraine. Among other tests and scales they also used the CTSIB and the DGI, concluding that vestibular migraine sufferers, defined according to the Lempert and Neuhauser criteria⁴, as well as the migraineurs without vertigo, presented subnormal static and dynamic balance, as well as increased fall risk (FR). Góes³¹ used a stabilometric test to assess the static equilibrium of migraine patients interictally. The stabilometric parameters did not differ between patients and controls. However, migraine with aura

Table 2. Distribution of the tests for the Vestibulo-ocular Reflex, Vestibulo-spinal Reflex and Fall Risk in 30 migraine patients and 30 controls, paired for age and sex.

Parameter	Group	Total (%)		Control Group		P-value*
	Migraine			Normal	Abnormal	
HIT	Normal	19	(63.3)	16	3	0.344
	Abnormal	11	(36.7)	7	4	
	Total (%)	30	(100.0)	23	7	
HST	Normal	28	(93.3)	28	0	0.248
	Abnormal	2	(6.7)	2	0	
	Total (%)	30	(100.0)	30	0	
DVA	Normal	17	(56.7)	13	4	0.267
	Abnormal	13	(43.3)	9	4	
	Total (%)	30	(100.0)	22	8	
SVV	Normal	26	(86.7)	23	3	1.000
	Abnormal	4	(13.3)	3	1	
	Total (%)	30	(100.0)	26	4	
mCTSIB	Normal	24	(80.0)	23	1	0.375
	Abnormal	6	(20.0)	4	2	
	Total (%)	30	(100.0)	27	3	
RTT	Normal	19	(63.3)	17	2	0.039
	Abnormal	11	(36.7)	10	1	
	Total (%)	30	(100.0)	27	3	
PPT	Normal	24	(80.0)	20	4	0.754
	Abnormal	6	(20.0)	6	0	
	Total (%)	30	(100.0)	26	4	
FT	Normal	13	(43.3)	8	5	0.302
	Abnormal	17	(56.7)	10	7	
	Total (%)	30	(100.0)	18	12	
TUG	Normal	29	(96.7)	29	0	0.479
	Abnormal	1	(3.3)	1	0	
	Total (%)	30	(100.0)	30	0	
5TSST	Normal	26	(86.7)	26	0	0.074
	Abnormal	4	(13.3)	4	0	
	Total (%)	30	(100.0)	30	0	
RFT	Normal	30	(100.0)	30	0	1.000
	Abnormal	0	0.0	0	0	
	Total (%)	30	(100.0)	30	0	
DGI	Normal	26	(86.7)	25	1	0.375
	Abnormal	4	(13.3)	4	0	
	Total (%)	30	(100.0)	29	1	
PT	Normal	26	(86.7)	26	0	0.074
	Abnormal	4	(13.3)	4	0	
	Total (%)	30	(100.0)	30	0	

HIT: Head Impulse Test; HST: Head Shaking Test; DVA: Dynamic Visual Acuity; SVV: Subjective Visual Vertical; MIT: Minimal Ice Test; mCTSIB: Modified Clinical Test of Sensory Interaction and Balance; RTT: Romberg Tandem Test; PPT: Past Pointing Test; FT: Fukuda Test; TUG: Time Up and Go; 5TSST: 5 Times Sit to Stand Test; FRT: Forward Reaching Test; DGI: Dynamic Gait Index; PT: Pull Test. * Chi-square test of McNemar.

patients showed a significantly greater lateral oscillation than migraineurs without aura. In our study, the RTT was the most sensitive test, pointing to a dysfunction of the static equilibrium in migraineurs. Given the clearly unfavorable result for RTT it is possible that the dysfunction in migraine would be greater in the VSR mechanisms specially involving proprioceptive impulses. In the m-CTSIB test, when the subject is placed on the foam, the proprioceptive influence to the postural reflex drops by approximately 60%⁷. Although the

patients had no anteroposterior imbalance predominance, the migraineurs had three times more abnormal tests than controls, indicating that in migraine the vestibular influence on the posture control is comparatively dysfunctional. It remains to be explained whether this is secondary to impaired neck and/or labyrinth abnormal reflexes in migraine, as they could modulate the muscular tonus. Stretch reflexes receive important contribution from vestibulo-spinal responses, proprioceptive signs from the trunk and neck, or both,

visual stimulus, and voluntary responses³². Therefore, it is possible the subnormal vestibular function in migraine could increase the FR by stretch reflexes impairment.

In patients, the FR tests pointed to a subtle fall tendency. Only one patient showed increased FR according to the TUG test. Four migraineurs (13.3%), showed increased FR in the 5TSST, while none of the controls exceeded this test time limits (10 and 14.2 seconds, according to age). According to the FRT none of the sixty examined subjects showed an increased

FR, indicating that the vestibular postural dysfunctions in migraine cannot be assessed by this test. Observing the FRT response in association with other vestibular-spinal tests we conclude that the anterior tilt does not seem to be particularly affected in migraine.

Given the clearly abnormal result for RTT in migraine patients, it is possible this disease impairs mainly VSR mechanisms, specially involving proprioceptive impulses. Since the RTT preferably tests a side-to-side control, our results are in line with the findings of Góes³¹, in which the lateral oscillation was greater in migraineurs examined by stabilometry.

In the DGI, 13.3% of patients had a score of less than 19 points, i.e. suggestive of increased FR, while only one control (3.3%) scored for increased FR. Since this test requires different skills, it may be more sensitive than other FR assessment methods. The PT also shows that migraineurs present postural difficulties in the anteroposterior direction. The anticipatory postural reflexes are specially important in the anteroposterior instability provoked by pulling the patient. The corporal shift deterioration is an important factor for gait dearrangement in the elderly³³, but this cannot justify the comparatively worse PT results in migraineurs as they were not old. The anteroposterior instability in migraine seems to be better assessed by the PT than by the FRT.

The weaknesses of this work are the relatively small sample, the relatively lower age of patients for FR assessment, the lack of a migraine with vestibular symptoms group and other primary headache groups, and a lack of subsequent testing to confirm results consistency. Due to the high variation of the so-called “vestibular migraine” and the pathophysiological uncertainties related to this diagnosis we believe such patients cannot be selected by reliable criteria yet. Ideally, longitudinal and interventional studies specifically designed to assess vestibular dysfunction in migraine should be performed. However, we are confident data are convincing to

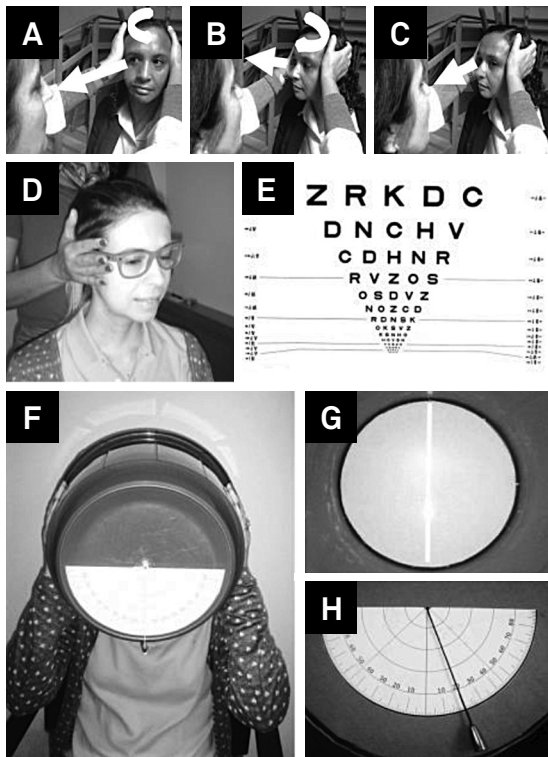


Figure 1. Vestibulo-ocular reflex tests. Head impulse test (A, B, C); dynamic visual acuity (D, E); subjective visual vertical (F, G, H).



Figure 2. Vestibulo-spinal reflex tests. Past pointing (A, B, C); m-CTSIB step 4 (D); Fukuda test (E, F). fall risk: pull test (G).

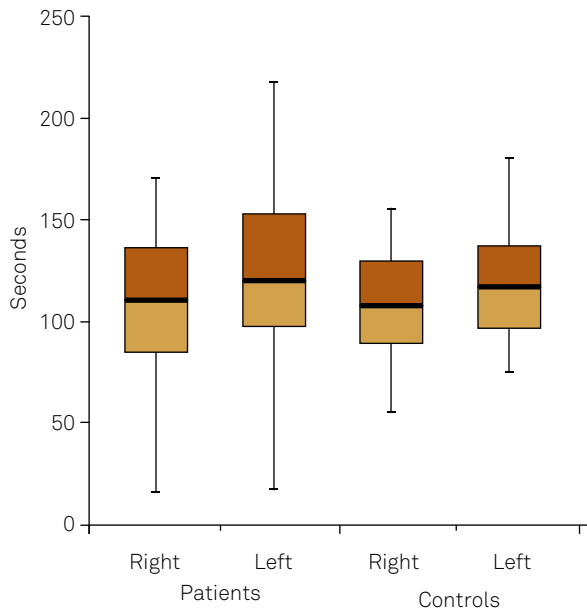


Figure 3. MIT. Patients and controls average nystagmus duration of caloric induced nystagmus in seconds. Box and whiskers plot showing the results of the MIT in seconds. Notice the greater response variability amongst patients. Box right (right ear), left (left ear).

Table 3. Power rating of discrimination scores between migraineurs and controls for different cutoff points.

Cutoff points*	Sensitivity	Specificity
1	96.7%	200%
2	70.0%	60.0%
3	50.0%	86.7%
4	23.3%	93.3%
5	20.0%	100.0%
6	10.0%	100.0%

* Positive for values higher or equal to score that counts the number of abnormal results in 13 tests.

demonstrate that migraineurs present subclinical vestibular dysfunctions that may be detected at the bedside. This is in line with the high prevalence of vertigo and unbalance complaints amongst migraineurs.

In conclusion, migraine patients consistently showed worse vestibulo-ocular, vestibulo-spinal and FR bedside tests as compared with controls. The results indicate that the vestibular function is impaired subclinically in migraine without vertigo complaints. Bedside tests are suitable to detect such dysfunctions. Whether these changes are specific for migraine headaches remains to be determined.

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