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Video head impulse test can detect brainstem dysfunction in multiple sclerosis

Ivan Pavlović[a,1], Berislav Ruška[a,1], Tin Pavičić[a,1], Magdalena Krbot Skorić[b], Luka Crnošija[a], Ivan Adamec[b], Mario Habek[a,b,*]

[a] University Hospital Center Zagreb, Department of Neurology, Referral Center for Autonomic Nervous System Disorders, Zagreb, Croatia
[b] School of Medicine, University of Zagreb, Zagreb, Croatia

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ABSTRACT

Background: The aim of this study was to investigate the potential role of video head impulse test (vHIT) in the detection of brainstem lesions in patients with multiple sclerosis (MS).
Methods: Sixty-eight participants were enrolled and divided into two groups: 39 healthy subjects (HC) (78 ears, 20 females, mean age 25,3 ± 6,3) and 29 MS patients (58 ears, 14 females, mean age 33,7 ± 7,7). Both groups underwent vHIT, and in MS group MRI was analyzed for the presence of brainstem lesions. vHIT pathology was defined as presence of overt saccades (< 200 ms) or lateral gain lower than 0.8 for lateral canal, and presence of overt saccades (< 200 ms) or posterior/anterior slope lower than 0.7.
Results: In HC, decreased gain on horizontal canals was found in 8 out of 78 ears (11%), while 16 out of 58 ears (38%) had pathological results in the MS group. Mean gain of the lateral canals (60 ms) was significantly reduced in MS group compared to HC (0.874 ± 0143 vs. 0.954 ± 0,170, $p = 0.004$, respectively). Compared to HC overt saccades < 200 ms in the lateral canals ($p = 0.018$) and in the posterior canals ($p = 0.011$), overt saccades > 200 ms in lateral ($p < 0.001$), anterior ($p = 0.019$) and posterior canals ($p = 0.009$), and covert saccades in the anterior ($p = 0.042$) and posterior canals ($p = 0.046$) were more frequent in the MS group. There was statistically significant association between the presence of BS MR lesions and bilateral pathology on vHIT for lateral semicircular canal ($\chi(1) = 3.982$, $p = 0.046$).
Conclusion: These results indicate that vHIT can detect brainstem dysfunction in patients with MS.

1. Introduction

Involvement of the brainstem in multiple sclerosis (MS) has significant implications on the disease course and can be presented with different symptoms amongst which are the ones associated with vestibular system. Lesions of vestibular system can be subclinical or present with equilibrium disorders such as vertigo and dizziness (Habek, 2013). There are many tests which are able to detect brainstem involvement in MS with various degrees of success (Magnano et al., 2014).

It has been shown that the video head impulse test (vHIT) is of great importance in evaluating the function of the peripheral vestibular system (MacDougall et al., 2009). vHIT uses head-mounted high-speed camera for tracking eye movements during short head impulses. Eye to head ratio measured by this device then enables clinicians to assess the main indicator of the peripheral vestibular function: vestibulo-ocular reflex (VOR) gain (MacDougall et al., 2009). Although primary use of vHIT is to make a distinction between peripheral and central vestibular disorders by detecting peripheral vestibular dysfunction, some researches have shown that VOR can also be impaired when central part of the vestibular system is damaged (Kim et al., 2014). With presumption that demyelinating lesions affecting central part of vestibular system could possibly cause impairment in VOR gain, we performed vHIT examination in patients with MS and compared their results with the ones of healthy subjects. Due to weak correlation between radiological extent of the disease measured by MRI and its clinical presentation (Barkhof, 2002), it is of great importance to find potential methods for testing brainstem involvement in MS patients. This study therefore investigates the potential role of vHIT in the detection of brainstem lesions in patients with MS.

* Correspondence to: University Department of Neurology, University Hospital Center Zagreb, Kišpatićeva 12, HR-10000 Zagreb, Croatia.
E-mail address: mhabek@mef.hr (M. Habek).
[1] These authors contributed equally.

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2. Materials and methods

In this case-control, prospective study, sixty-eight participants underwent vHIT testing from March 2016 to November 2016 at the University Hospital Center Zagreb, Croatia. Participants were divided into two groups, a group of healthy control subjects (HC) (78 ears, 20 females, mean age 25,3 ± 6,3) and a group of patients previously diagnosed with relapsing remitting multiple sclerosis (MS) (58 ears, 14 females, mean age 33,7 ± 7,7) according to the revised McDonald criteria (Polman et al., 2011). All patients performed routine MRI within 30 days prior to vHIT. In both groups presence of peripheral vestibular disorder was excluded by history taking and clinical examination. Furthermore, it was ensured that subjects were not taking medications known to affect the vestibular system (tranquilizers, sedatives, vestibular suppressants).

MRIs performed on a 1.5 T MRI scanner were considered eligible. Brainstem multi-planar dual fast spin-echo PD and T2-WI sequences were analyzed for presence of demyelinating lesions in the brainstem as a whole. All MRIs were reviewed by two independent investigators who were blinded for patients' symptoms and vHIT results at the time of analysis, and only lesions identified by both investigators were considered as present.

The protocol was approved by the ethical committee of the University Hospital Center Zagreb. Before the study, the protocol was explained and discussed with the participants and they all signed informed consent. Video head impulse test has already been described in great detail by MacDougall and Curthoys (MacDougall et al., 2009; Curthoys et al., 2014). The system used in this study was the Eye-SeeCam vHIT (Interacoustics, 5500 Middlefart, Denmark). The system consists of a small high-quality camera which focuses the left eye and is mounted on the frame of the goggles. After placing the participant 1.5 m in front of the eye-leveled target (Mossman et al., 2015) and checking whether all the necessary head movements are doable and painless without complications, the goggles with an elastic band are comfortably locked onto the subject's head. The goggles were locked tightly onto the bridge of the nose and around the eye sockets in order to reduce the slippage to the minimum, therefore decreasing the chance of the artifacts occurrence. In order to assure the pupil is accurately tracked, the subject was instructed to keep the eyes widely open and to blink as less as possible. Calibration was performed for the eyes and head movements prior to formal testing. The VOR was generated through the rotation of the subjects head unpredictable in direction and time (peak head velocity 150°/s to 300°/s) by the examiner. The impulses of the head were delivered in 3 planes: lateral, right anterior-left posterior (RALP) and left anterior-right posterior (LARP) with a minimum of 5 head impulses in each plane and direction.

Following vHIT parameters were analyzed: for the right and left lateral canals gain at 60 ms, presence of covert and overt saccades and gain asymmetry. For right anterior (RA), left posterior (LP), left anterior (LA) and right posterior (RP) slope and presence of covert and overt saccades. Gain, slope and asymmetry were automatically calculated by OtoAccess. Each test was visually inspected for presence of saccades. vHIT pathology was defined by the presence of overt saccades (< 200 ms) or lateral gain lower than 0.8 for lateral canals, and presence of overt saccades (< 200 ms) or posterior/anterior slope lower than 0.7 for anterior and posterior canals (Yang et al., 2016).

The primary outcome was comparison of vHIT results in subjects diagnosed with MS and the healthy control group.

Secondary outcome was to correlate pathological findings of vHIT with the existence of brainstem lesions visible on MRI in subjects with MS.

Statistical analysis was performed using the IBM SPSS software, version 20. The Kolmogorov-Smirnov test was applied to test whether the data have a normal distribution. Differences in the distribution of qualitative variables were determined with the χ^2 test, while the differences in quantitative variables were determined with independent sample *t*-test. P values less than 0.05 were considered significant.

Table 1
Results of vHIT parameters and differences between groups.

vHIT parameter	Group	Mean	SD	p value
Lateral canal gain (40 ms)	MS	1.018	0.214	0.010
	HC	1.126	0.256	
Lateral canal (60 ms)	MS	0.874	0.143	0.004
	HC	0.954	0.170	
Lateral canal (80 ms)	MS	0.850	0.137	0.088
	HC	0.888	0.120	
Anterior canal slope	MS	1.249	0.607	0.264
	HC	1.153	0.282	
Posterior canal slope	MS	1.009	0.438	0.140
	HC	1.110	0.360	

3. Results

Results of vHIT parameters and differences between groups are presented in Table 1.

Compared to healthy controls overt saccades < 200 ms in the lateral canals (p = 0.018) and in the posterior canals (p = 0.011), overt saccades > 200 ms in lateral (p < 0.001), anterior (p = 0.019) and posterior canals (p = 0.009), and covert saccades in the anterior (p = 0.042) and posterior canals (p = 0.046) were more frequent in the MS group. The distribution of subjects in MS and HC group according to the pathological findings of vHIT gains/slopes (if we use the cut off values for lateral canal gain at 60 ms of 0.8 and for the anterior and posterior canal slope 0.7) are presented in Table 2.

Finally, results were considered pathological if there was presence of overt saccades (< 200 ms) or lateral gain lower than 0.8 for lateral semicircular canal, and presence of overt saccades (< 200 ms) or posterior/anterior slope lower than 0.7 for posterior/anterior semicircular canal. Bilateral pathology was regarded as presence of pathological responses on both sides for specific semicircular canal. Six patients had bilateral pathology on lateral canals and all of them had BS lesions evident on MRI. Analysis showed that there is statistically significant association between the presence of BS MRI lesions and bilateral pathology on vHIT for lateral semicircular canals ($\chi(1) = 3.982$, p = 0.046). The example of a patient with brainstem lesions and bilateral vHIT pathology is presented in Fig. 1.

4. Discussion

The main finding of this study was a significantly more frequent pathological vHIT test in patients diagnosed with MS compared to healthy controls. Furthermore, we have shown that bilaterally pathologic vHIT finding can detect brainstem lesions in MS. This finding is of

Table 2
The distribution of subjects in MS and HC group according to the pathological findings of vHIT gains/slopes (if we use the cut off values for lateral canal gain at 60 ms of 0.8 and for the anterior and posterior canal slope 0.7).

vHIT parameter	Group	Pathological value of the vHIT parameter		p value
		No	Yes	
Lateral canal (60 ms)	MS	42	16	0.009
	HC	70	8	
Anterior canal slope	MS	51	7	0.027
	HC	76	2	
Posterior canal slope	MS	47	11	0.004
	HC	75	3	