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Ocular and cervical vestibular evoked myogenic potentials in multiple sclerosis patients

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HIGHLIGHTS

- Multiple sclerosis patients showed high frequency of abnormality in vestibular evoked myogenic potentials (VEMPs) tests, especially in ocular VEMP tests.
- VEMP abnormalities were not correlated with brainstem clinical or magnetic resonance imaging lesions.
- VEMP abnormalities were significantly correlated with expanded disability status scale (EDSS).

ABSTRACT

Objective: Vestibular evoked myogenic potentials (VEMPs) are thought to provide useful information about brainstem functions, as the neural pathways of both ocular and cervical VEMPs pass through the brainstem. The aim of this study was to investigate the clinical value of ocular and cervical VEMP tests in the evaluation of brainstem involvement in multiple sclerosis (MS) patients and to assess their relation with clinical and cranial MRI findings.
Methods: Ocular and cervical VEMPs were recorded in 62 MS patients and 35 age and sex matched healthy volunteers. The latencies, amplitude asymmetry ratios of both VEMP responses and abnormality ratios (prolonged latencies and absent responses) were compared between the MS patients and the control group and among the groups of MS patients.
Results: oVEMP mean n1 and p1 latencies and cVEMP mean p13 latency were significantly prolonged in MS patients. Although the abnormality ratios of both VEMPs were higher in patients with brainstem clinical or MRI lesions, the correlation was not statistically significant. Both ocular and cervical VEMP latencies were significantly correlated with expanded disability status scale.
Conclusions: Although there is no significant correlation with clinical or MRI findings, MS patients show high frequency of abnormality in VEMP tests, especially in oVEMP tests.
Significance: VEMP tests may be useful as an adjunct test in the evaluation of brainstem dysfunction in MS patients.

1. Introduction

Multiple sclerosis (MS) is a chronic demyelinating disease involving the white matter of the central nervous system. The signs and symptoms of the disease, clinical course and response to treatment are different in every case. Although magnetic resonance imaging (MRI) is the most important test in the diagnosis of MS, besides being an objective indicator of involvement of the related pathways, evoked potentials are also important in the diagnosis of MS in terms of demonstrating subclinical demyelination (Chiappa, 1984; Comi et al., 1999; Fuhr and Kappos, 2001).

Vestibular evoked myogenic potentials (VEMPs) are short latency electromyographic (EMG) responses that can be recorded from various muscles during the contraction phase in response to acoustic stimulus (Debatisse et al., 2005; Rosengren et al., 2010; Akin et al., 2004; Zhou and Cox, 2004; Brantberg, 2009; Cherchi et al., 2009). VEMPs recorded from ipsilateral SCM muscle known

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as "cervical VEMP" (cVEMP) are a clinical demonstration of vestibulo-collic reflex (Rosengren et al., 2010; Brantberg, 2009; Park et al., 2010). The cVEMP pathway is believed to originate in the saccular macula and continues through the vestibular nerve and nucleus, the vestibulospinal tracts, spinal motor nucleus and SCM muscles (Rosengren et al., 2010; Park et al., 2010; Bektas et al., 2008). cVEMP responses are characterized by biphasic waves with initial positivity (p13) followed by a negative wave (n23). Recently, myogenic response recorded from contralateral extraocular muscles in response to acoustic stimuli has been reported to be a manifestation of crossed vestibulo-ocular reflex and named "ocular VEMP" (oVEMP). The oVEMP pathway is thought to travel through the medial longitudinal fasciculus (MLF), the oculomotor nuclei and nerves and the extraocular muscles after the activation of the vestibular nerve and nucleus (Rosengren et al., 2010). oVEMP responses are characterized by biphasic waves with an initial negative peak (n1) followed by a positive peak (p1).

The cVEMP test has become an important diagnostic tool, particularly in the evaluation of peripheral vestibular disorders. VEMPs are thought to provide useful information about brainstem functions, as the neural pathway of both VEMPs pass through the brainstem. While cVEMP descends via the vestibulospinal tract through the lower brainstem, oVEMP ascends via the MLF through the upper brainstem (Rosengren et al., 2007, 2010; Itoh et al., 2001; Tu and Young, 2004; Eleftheriadou et al., 2009; Lin et al., 2010).

Several studies have described cVEMP abnormalities in brainstem lesions, including research with MS patients (Itoh et al., 2001; Versino et al., 2002; Patko et al., 2007; Shimizu et al., 2000; Sartucci and Logi, 2002; Pollak et al., 2006; Bandini et al., 2004; Alpini et al., 2004; Aidar and Suzuki, 2005). There are only a few reports about the diagnostic value of oVEMP in brainstem lesions (Rosengren et al., 2007; Rosengren and Colebatch, 2011; Su and Young, 2011). But none has evaluated the correlation of oVEMP tests with both current and past clinical and MRI findings of MS patients.

We aimed to investigate the clinical value of ocular and cervical VEMP tests in the evaluation of brainstem involvement in MS patients and their value in detecting silent brainstem lesions and to assess their relations with clinical and cranial MRI findings.

2. Methods

2.1. Subjects

Sixty-two patients with definite MS according to the McDonald criteria and 35 healthy volunteers were included (Polman et al., 2005). All patients were examined using otoscopy and audiometric testing before the study. Subjects with abnormal audiometric tests and limited neck movements were excluded. The ethical committee approved the study, and informed consent was obtained from each subject.

2.2. Clinical and MRI examinations

All patients were questioned and examined for current brainstem or cerebellar clinical involvement. Previous brainstem or cerebellar clinical involvement of all patients was noted from their medical records.

Patients were then divided into groups according to the presence of current or past brainstem and cerebellar clinical involvement. Both symptoms and signs were taken into consideration while grouping patients. Patients with vertigo were grouped according to the presence of additional brainstem or cerebellar clinical findings. No additional test (caloric test, head shaking test, etc.) was required since none of the patients had any findings suggestive of vestibular dysfunction at neurological examination. Symptoms and signs within 3 months before VEMP testing were considered as current, and those appearing more than 3 months previously at any time during the course of the disease, and that improved and were not observed within the previous 3 months were considered as past brainstem and cerebellar clinical involvement.

All previous and current MRI scans of each patient performed since the onset of the disease were reviewed for current and past brainstem or cerebellar lesions. Twenty patients who did not have an MRI within 3 months before VEMP testing were excluded. Brain MRI scans were evaluated by another examiner blinded to patients' previous and current clinical findings. Brain lesions were described as being localized to the right or left mesencephalon, pons, medulla and cerebellum. Brain lesions seen at MRI within 3 months before VEMP testing were considered as current lesions. Brain lesions seen on previous MRI scans but not observed on MRI scans within the previous 3 months were considered as past lesions.

2.3. VEMP recordings

VEMP tests were performed on the same day as the clinical examination by a different examiner blinded to the groups and patients' clinical and MRI examinations.

VEMP recordings were performed using a Medelec Synergy EMG/EP machine (Oxford Instruments Medical, Surrey, UK). Patients were tested in a sitting position. EMG signals were amplified and band pass-filtered between 1 and 1000 Hz. We used sound stimuli presented through headphones as rarefaction clicks of 0.1 ms duration and a frequency of 5 Hz. A total of 128 stimuli were applied to each ear and repeated two consecutive times at an intensity of 105 dB nHL. Click stimulus was preferred over low frequency tone-burst due to the problems in generating short tone burst in our laboratory.

For the cVEMP test, active electrode was placed on the upper one-third of the SCM ipsilateral to the sound stimulation, with the reference electrode on the anterior margin of the clavicle and the ground electrode on the forehead. Patients were asked to turn their heads contralaterally to activate the ipsilateral SCM muscle and to hold this position throughout the recording period. Muscle activation was monitored during the recording and maintained at a constant level (>50 μV). Peak latencies of p13 and n23 and peak-to-peak amplitudes (p13-n23) were measured. The interside differences of p13 and n23 latency and amplitude asymmetry ratio (AR) were calculated. AR was calculated as follows: (larger response-smaller response)/(larger response + smaller response) × 100 (Rosengren et al., 2010) We preferred to use AR for the interpretation of the VEMP amplitude, since VEMP response amplitude is significantly affected by the force of muscular contraction or stimulus intensity and exhibits wide variation.

For the oVEMP test, active electrode was placed around 1 cm below the center of the inferior eyelid contralateral to the sound stimulation, with the reference electrode 15 mm below the active one and the ground electrode on the forehead. During the test, patients were asked to look upward to a fixed point 2 m distant and 30–35° above the horizontal line. The peak latencies of n1, p1 and peak-to-peak amplitudes (n1-p1) were measured. The interside differences of n1 and p1 latency and AR were calculated.

2.4. Statistical analysis

Statistical analysis was performed using SPSS for Windows version 15. Means and standard deviations of each VEMP parameter were determined. After evaluation of the assumption of the normal distribution, student's *t* test was applied to compare continuous