Cervical and ocular vestibular evoked myogenic potentials in multiple sclerosis participants

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Abstract
Background: Multiple sclerosis (MS) is a chronic neurological disease that affects brain and spinal cord. The infratentorial region contains the cerebellum and brainstem. Vestibular evoked myogenic potentials (VEMPs) are short-latency myogenic responses. Cervical vestibular evoked myogenic potential (cVEMP) is a manifestation of vestibulocolic reflex and ocular vestibular evoked myogenic potential (oVEMP) contributes to the linear vestibular–ocular reflex. The aim of this study was to evaluate cVEMP and oVEMP in MS patients with and without infratentorial plaques and compare the findings with normal controls.

Methods: In this cross-sectional study, latency and amplitude of cVEMP and oVEMP were recorded in 15 healthy females with mean age of 31.13±9.27 years, 17 female MS patients with infratentorial plaque(s) and mean age of 29.88±8.93 years, and 17 female MS patients without infratentorial plaque(s) and mean age of 30.58±8.02 years. All patients underwent a complete clinical neurological evaluation and brain MRI scanning. Simple random sampling method was used in this study and data were analyzed using one way ANOVA through SPSS v22.

Results: The latency of N1-P1 and P13 in MS participants with and without infratentorial plaques were significantly prolonged compared to normal controls (p<0.001). Additionally latency of P13-N23-N1 and P1 in MS patients with infratentorial plaques were significantly prolonged compared to patients without infratentorial plaques subjects (p<0.001).

Conclusion: Abnormality of both cVEMP and oVEMP in MS patient with infratentorial plaque are more than that of MS patient without infratentorial plaque. Recording both ocular and cervical VEMPs are appropriate electrophysiologic methods assessing the function of both ascending and descending central vestibular pathways.

Keywords: Multiple sclerosis, Cervical, ocular, Vestibular evoked myogenic potential, Infratentorial plaque.


Introduction
Multiple sclerosis (MS) is a chronic neurological disease that affects brain and spinal cord. Most people are diagnosed between the ages of 20-40. It is estimated that women are affected three times more than men (1).

MS damages the myelin sheath involving the white matters of central nervous system. Tentorial incisure (also known as the tentorial notch or incisura tentorii) refers to an extension of one of the membranes covering the cerebrum which, with the transverse fissure, separates the cerebrum from...
the cerebellum. The infratentorial region of
the brain is the area located below the ten-
torium cerebelli. The infratentorial region
contains the cerebellum and brainstem (2,
3).

Evoked potentials play an important role
in the diagnosis and follow up of MS. They
can detect subclinical lesions and provide
information on the function of different
parts of the nervous system (4).

Vestibular evoked myogenic potentials
(VEMPs) are short-latency myogenic re-
ponses which are evoked by brief pulses
of air conducted (AC) acoustic signals,
bone conducted (BC) vibration or electrical
stimulus. VEMPs are recorded via surface
electrodes over surface of muscles such as
sternocleidomastoid (SCM) (5). Cervical
vestibular evoked myogenic potential
cVEMP) was first described by Colebatch
et al (1992), and now has become an ac-
cepted test of vestibular functions. The
cVEMPs are recorded from the SCM or
trapezius muscles (5). It is a manifestation
of vestibulocolic reflex. An auditory tone
burst stimulation leads to activation of the
saccular vestibular neurons, which in turn
cause a modulation of tonic muscle activity
of the SCM muscle. The measurement of
the VEMPs requires tonic contraction of
ipsilateral SCM muscle (6). The cVEMP
response has two main peaks, labeled P13
and N23 (7).

In recent decade VEMPs have been re-
corded from the extraocular muscles (ocular
or oVEMP) (8, 9). In this test loud acousti-
cal stimuli produce vestibular dependent
responses in the extraocular muscles. The
responses are believed to be originated
from the otoliths and they contributed to
the linear vestibular–ocular reflex (10). The
primary oVEMP projection appears to be
crossed and the initial negative peak oc-
curred at about 10 ms.

Studies have shown infratentorial plays
an important role in the transition, percep-
tion and interpretation of vestibular infor-
mation and also both the vestibule-ocular
and vestibulocolic pathways pass from this
area. Therefore, the lesions in this region
can significantly impact on the balance and
cVEMP and oVEMP. Since the impact of
plaque(s) in the infratentorial on the
cVEMP and oVEMP is not investigated,
the aim of this study was to compare cervi-
cal and ocular vestibular evoked myogenic
potentials in multiple sclerosis patients with
and without infratentorial plaque(s) and
compare the findings with normal controls.

Methods

In this cross- sectional study cVEMP and
oVEMP were performed on 15 healthy fe-
male subjects with mean age of 31.13±9.27
years, 17 female patients with definite MS
according to the MC Donald criteria 2005,
with infratentorial plaque(s) with mean age
of 29.88±8.93 years and 17 female MS pa-
ients with definite MS without infratento-
rial plaque(s) with mean age of 30.58±8.02
years.

MC Donald criteria 2005 incorporated
magnetic resonance imaging (MRI) into the
well-established diagnostic workup that
focuses on detailed neurological history
and examination and a variety of paracli-
nical laboratory examinations such as cere-
brospihal fluid analysis (11, 12).

All tests of the present study did from Oc-
tober to December 2013 in Tehran Univer-
sity of Medical Science.

All participants were evaluated using
otoscopy and audiometric testing before
study. Subjects with abnormal audiometric
results (hearing thresholds worse than 20
dB HL)(13), with a history of seizures, de-
pression, and head trauma and neck or eye
movement limitation like strabismus and
cervical arthritis were excluded. All pa-
ients underwent a complete clinical neuro-
logical evaluation and brain MRI scanning
within three weeks. Then patients were di-
vided into two groups consisting of patients
with and without infratentorial plaque(s).

To record cVEMPs, subjects were sat on
a comfortable chair, turned their head op-
posite to the side of the stimulated ear in
order to flex the SCM muscle. Contraction
of SCM muscle was monitored with ma-
nometer. In this way subjects pushing with
their jaw against the hand-held inflated cuff to generate a 40 millimeter of mercury cuff pressure (14). After cleaning the skin active surface electrode was placed on the upper half of each SCM muscle with a reference electrode over the upper sternum and a ground electrode over central forehead (15) (Figure1). Cervical VEMPs were recorded from ipsilateral SCM muscle (from the stimulated side) in response to AC 500 Hz short tone burst delivered via insert earphones at 95 dB nHL. Both cVEMP & oVEMP were performed using GN Otometric-ICS CHARTER EP.

Data were analyzed using one way ANOVA and paired t-test because the distribution of data was normal according to the Kolmogrov-Smirnov test and p<0.05 was considered statistically significant. SPSS software version 22 was used in this study. Tehran University of Medical Sciences Ethical Committee approved this study, and informal consent was obtained from each subjects.

Results
The mean latency and amplitude of P13, N23, N1 and P1 in all participants have been showed in Table 1. Sample of cVEMPs and oVEMPs in three groups are shown in Fig. 2.

In the control group cVEMPs and oVEMP were recorded from both sides of all participants. Analysis showed no significant differences between the mean latency and amplitude of P13, N23, N1 and P1 in

<table>
<thead>
<tr>
<th>Group</th>
<th>Tests</th>
<th>Peaks</th>
<th>Latency (ms)</th>
<th>Amplitude(µV)</th>
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<td>Left (Mean±(SD))</td>
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<td>oVEMP</td>
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<td></td>
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<td>N1</td>
<td>24/48±1/18</td>
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<tr>
<td>MS without infra tentorial plaque</td>
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<td>P13</td>
<td>17/44±1/03</td>
<td>17/21±1/05</td>
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<td></td>
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<td>133/78±22/89</td>
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<tr>
<td>MS with infra tentorial plaque</td>
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<td>P13</td>
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<td></td>
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<td>15/74±1/66</td>
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<tr>
<td></td>
<td></td>
<td>P1</td>
<td>20/59±1/65</td>
<td>21/40±2/88</td>
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Table 1. Descriptive statistics of oVEMP and cVEMP in all groups

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right and left side (p>0.05).

In multiple sclerosis patients without infratentorial plaques cVEMPs were recorded from both sides of all patients but oVEMP were recorded from both sides in 64.7% (n=11) patients and recorded from one side in 11% (n=2) patients and not recorded bilaterally in 23.5% patients (n=4). Statistical analysis showed no significant differences between the mean latency and amplitude of P13, N23, N1 and P1 in right and left side (p>0.05).

In multiple sclerosis patients with infratentorial plaques cVEMPs were recorded from both sides in 59.0% (n=10) of patients and from one side in 17% (n=3) of patients and not recorded in 23.5% (n=4) of patients. Ocular VEMPs were recorded from both sides in 23.5% (n=4) of patients and recorded from one side in 23.5% (n=4) of patients.

Fig. 2. Sample of cVEMPs and oVEMPs in control group (A&B), in MS patients without infratentorial plaques (C&D) and in MS patients with infratentorial plaques (E&F).
patients and not recorded in 52.59% (n=9) of patients. Analysis showed no significant differences between the mean latency and amplitude of P13, N23, N1 and P1 in right and left side (p>0.05).

Statistical analysis showed the latency of N1, P1 and P13 in multiple sclerosis with and without infratentorial plaques were significantly prolonged compared to normal controls (p<0.001). Also latency of P13, N23, N1 and P1 in MS patients with infratentorial plaques were significantly prolonged compared to patients without infratentorial plaques subjects (p<0.001). There was no significant difference in the mean amplitude of both oVEMP & cVEMP between MS patients with infratentorial plaque(s) and MS patients without infratentorial plaque(s) (p>0.05).

Discussion

The aim of the present study was to evaluate cVEMP & oVEMP in MS patients with and without infratentorial plaques and compare the findings with normal controls.

The latency of N1-P1-P13 were significantly longer in MS patients with and without infratentorial plaque(s) compared to control subjects and latency of P13-N23-N1&P1 in MS patients with infratentorial plaques were significantly prolonged compared to patients without infratentorial plaques. Prolonged latency of VEMPs in MS patients has been reported in previous studies (18-21). Only latency of N23peak of MS patient without infratentorial plaque(s) was not significantly different compared to normal controls probably because of larger normal limits which has been reported in previous studies (21). Prolonged latency of VEMPs are not specific for MS and cannot help distinguish MS from other etiologies (18, 22, 23). Delays of latency in VEMPs have been seen in other neurological disease that affecting brainstem such as stroke and tumors(24).

Overall in the present study 64.25% had some form of cVEMP abnormality and 85.66% had some form of oVEMP abnormality in MS patients with infratentorial plaque(s). In MS patients without infratentorial plaque(s) abnormality of cVEMP & oVEMP were seen in 18.26% and 45.28% of patients, respectively. Data showed ocular VEMPs are often abnormal in patients with infratentorial plaques, because ocular VEMP pathway passes through the brainstem which is in the infratentorial zone. The abnormality percentage of oVEMPs was higher than that of the cVEMPs in our study in both MS patient groups. Our results showed that oVEMPs is more sensitive than cVEMPs in MS(18, 20).

VEMPs are capable to demonstrate subclinical dysfunctions or silent lesions. In MS patients without infratentorial plaque(s) 43.23% of cVEMP and 61.48% oVEMP were abnormal. Clinically silent lesions can explain physiologic changes that are not accompanied by physical signs or symptoms. Perhaps small demyelinating lesions not detected by MRI can produce slow nerve conduction velocity (18, 19, 21, 23). VEMPs can also demonstrate clinical dysfunction. In this study cVEMP abnormalities were seen in 73.43% and oVEMP abnormalities were seen in 94.11% of MS patients with infratentorial plaque(s). Most common abnormality found in MS patients with infratentorial plaque(s) was absent response and the other abnormality was latency prolongation. Demyelination can cause speed reduction which can result in slow nerve conduction velocity. However severe demyelinating lesions can cause conduction block or desynchronized conduction (19, 21).

There were no statistically significant differences between the mean amplitude of cVEMP and oVEMP of both MS groups with normal subjects. This VEMP parameter in MS patient is not a proper diagnostic criteria because other variables such as muscle contraction and stimulus intensity can affect it (18, 23, 25). Amplitudes of VEMPs responses should not be used alone and should be interpreted together with latency values in MS patients (23).

Conclusion
Findings of the current study showed that abnormality of both cVEMP and oVEMP in MS patient with infratentorial plaque are more than that of MS patient without infratentorial plaque. Recording both ocular and cervical VEMPs are appropriate electrophysiological methods assessing the function of both ascending and descending central vestibular pathways in diagnosis, monitoring disease progression and rehabilitation in MS patients.

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