Vibration- and Hyperventilation-Induced Nystagmus in Patients with Ramsay Hunt Syndrome with Vertigo

Chang-Hee Kim, MD, PhD1, Kyung-Hwa Jeong, MD1, Sung Hwan Ahn, MD1, Dong Hyuk Shin, MD1, Yong Won Kim, MD1, and Jung Eun Shin, MD, PhD1

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

Abstract
Objectives. The aims of this study were to compare vibration-induced nystagmus (VIN) and hyperventilation-induced nystagmus (HVIN) findings in patients with Ramsay Hunt syndrome with vertigo (RHS-V), sudden sensorineural hearing loss with vertigo (SSNHL-V), and vestibular neuritis (VN) during the acute stage and to address the possible lesion sites of vestibular deficit in RHS-V.

Study Design. Case series with chart review.

Setting. Tertiary referral center.

Methods. We conducted a retrospective case series study in 27 patients with SSNHL-V, 104 patients with VN, and 17 patients with RHS-V and evaluated the findings of VIN and HVIN tests.

Results. An abnormal VIN was observed in 91% of the patients with VN, 89% of those with SSNHL-V, and 94% of those with RHS-V, and the prevalence of abnormal VIN was not significantly different (P = .436). An abnormal HVIN was observed in 51% of the patients with VN, 22% of those with SSNHL-V, and 59% of those with RHS-V. While the prevalence of an abnormal HVIN was significantly different between SSNHL-V and VN groups (P = .007) and between SSNHL-V and RHS-V groups (P = .014), that between VN and RHS-V groups did not show a significant difference (P = .547).

Conclusion. Since the results of HVIN in RHS-V patients were more similar to those in VN patients than those in SSNHL-V patients, a lesioned site may be more likely within the vestibular nerve than the inner ear as a cause for vestibular deficit in patients with RHS-V who show caloric canal paresis of 25% or greater.

Keywords
Ramsay Hunt syndrome, sudden sensorineural hearing loss, vertigo, vestibular neuritis, vibration-induced nystagmus, hyperventilation-induced nystagmus

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Vestibular neuritis (VN), sudden sensorineural hearing loss with vertigo (SSNHL-V), and Ramsay Hunt syndrome with vertigo (RHS-V) are common causes of acute spontaneous vertigo with a peripheral origin. VN is characterized by a sudden unilateral and peripheral vestibular deficit without an associated hearing loss. The lesioned site in VN is believed to be located in the vestibular nerve, of which a superior branch is predominantly involved.1 SSNHL-V is characterized by a sudden peripheral vestibular deficit with an accompanying sensorineural hearing loss of 30 dB or more covering at least 3 contiguous audiometric frequencies that occurs within 3 days or less. Although the cause of SSNHL-V is still controversial, a peripheral end organ is thought to be the site of the abnormality.2,3 RHS-V is characterized by symptoms of otalgia, auricular vesicles, peripheral facial palsy, and vertigo. The lesioned site responsible for the vestibular deficit in RHS-V remains controversial; however, previous studies suggested the vestibular nerve,4-6 labyrinth,7 or both8 as possible sites of the lesion. As observed in a previous study that showed different findings of vestibular function between VN and SSNHL-V,9 characteristics of the vestibular deficit would be distinct according to the lesion of vestibular involvement among patients with VN, SSNHL-V, and RHS-V.

Hyperventilation may induce nystagmus (hyperventilation-induced nystagmus, HVIN) by unmasking the underlying vestibular asymmetry in various vestibulopathies, including central and peripheral disorders.10 Vibratory stimulation of the mastoid

1Department of Otorhinolaryngology—Head and Neck Surgery, Konkuk University Medical Center, Konkuk University School of Medicine, Seoul, South Korea

Corresponding Author:
Chang-Hee Kim, MD, PhD, Department of Otorhinolaryngology—Head & Neck Surgery, Konkuk University Medical Center, Konkuk University School of Medicine, 120-1 Neungdong-ro (Hwayang-dong), Gwangjin-gu, Seoul, 143-729, Korea.
Email: 20110552@kuh.ac.kr
bone or the sternocleidomastoid muscle may elicit nystagmus (vibration-induced nystagmus, VIN) in patients with unilateral vestibular disorders. While the findings of VIN and HVIN are well documented in patients with VN, the effects of vibration or hyperventilation have not been adequately investigated in patients with SSNHL-V and RHS-V. The aims of this study were to elucidate the differences in the prevalence and characteristics of VIN and HVIN among patients with VN, SSNHL-V, and RHS-V and to address the possible lesion sites in each disease.

Subjects and Methods

Subjects

We retrospectively evaluated 27 patients (11 men and 16 women; mean age, 55 ± 14 years) with SSNHL-V, 104 patients (54 men and 50 women; mean age, 51 ± 12 years) with VN, and 17 patients (7 men and 10 women; mean age, 55 ± 14 years) with RHS-V between March 2009 and March 2013.

The patients with SSNHL met the clinical diagnostic criteria for SSNHL, which is defined as a sensorineural hearing loss of 30 dB or more over at least 3 contiguous frequencies that develops within 3 days. The diagnostic criteria for SSNHL-V included SSNHL accompanied by a sudden attack of rotatory vertigo without any other neurological signs. The vertigo attack occurred almost simultaneously with the onset of hearing loss (within a day). The patients exhibiting canal paresis (CP) of 25% or greater in a caloric test were included in this study, and those who experienced multiple previous attacks of vertigo or accompanying benign paroxysmal positional vertigo were excluded from the study.

The diagnostic criteria for VN include sudden onset of vertigo, for more than 1 day, with unidirectional spontaneous horizontal nystagmus, absence of other auditory and neurological findings, reduced caloric response (CP ≥ 25%), and no history of vertigo or other neurotologic diseases. Brain magnetic resonance imaging (MRI) did not reveal acute infarction or other acute/chronic brain lesions, including cerebellar pontine angle tumors, in any of the patients. Patients with interaural differences of more than 15 dB were excluded from the study.

The diagnosis of RHS-V was based on typical clinical signs, such as auricular vesicles, facial palsy, and vertigo. Among these, patients exhibiting a CP of 25% or greater in a caloric test were included in this study. Sixteen (of 17, 94%) patients with RHS-V also complained of audiologic symptoms such as hearing loss, tinnitus, or ear fullness, and pure tone audiometry revealed sensorineural hearing loss on the affected side in these 16 patients.

The patients included in this study did not report a history of neurotologic disorders or otologic surgery in the affected and unaffected ears. An experienced vestibular technician performed the vestibular tests within 10 days of the onset of vertigo. The Institutional Review Board of Konkuk University Medical Center approved the study (KUH1110039).

Vestibular Function Tests

The VIN test was conducted using a hand-held vibrator (VVIB 100; Synapsys, France) with a fixed frequency of 100 Hz. Eye movements were recorded for 10 seconds during vibratory stimulation with patients in a sitting position; an infrared video-based system was used (CHARTR VNG, ICS Medical, Schaumberg, IL). Maximum slow-phase velocity (SPV) was calculated while vibration was applied to both mastoid bones and sternocleidomastoid (SCM) muscles. The fastest SPV on the horizontal plane during the vibratory stimulus was considered as the SPV of VIN. When spontaneous nystagmus was present, it was subtracted from the SPV of VIN. It was considered abnormal if all the SPVs from the 4 different stimulation sites were ≥ 2/s or greater or if SPVs from both mastoid bones and SCM muscles were ≥ 5/s or greater, which were obtained from our healthy volunteers. In patients with an abnormal VIN, the average SPV value (SPVavr) of SPVs obtained from vibrating right and left mastoid bones was calculated and used for further analysis.

A bithermal caloric test was performed, while recording eye movements, using an infrared video-based system (CHARTR VNG). Each ear was irrigated with a constant flow of water at alternating temperatures of 30°C and 44°C for a constant period of time (30 seconds). The maximum SPV of nystagmus was calculated following each irrigation, and Jongkees’ formula was used to determine CP. A CP ≥ 25% was considered abnormal.

For HVIN, the patients were asked to take deep and rapid breaths with their mouths open. The patients were instructed to ensure deep and rapid breathing for 90 seconds. When spontaneous nystagmus was present, it was subtracted from the SPV of HVIN. A positive test was defined as a maximum SPV of HVIN of ≥ 4/s. The use of the terms ipsilesional and contralesional indicates the direction of the quick phases of the induced nystagmus toward the lesioned side or intact side, respectively.

Only the horizontal component of VIN or HVIN was analyzed in this study.

Statistics

A comparison of CP between different disease groups was performed using a 1-way analysis of variance (ANOVA) with a post hoc Scheffe’s test. SPVs or CP values were compared between ipsilesional and contralesional HVIN in patients with VN using a t test for unpaired observations. We used linear regression to determine the significance of the correlation between CP and the SPVavr of VIN. Chi-square (χ²) or Fisher’s exact test was used to compare the prevalence of an abnormal VIN or HVIN among patients with VN, SSNHL-V, and RHS-V. P < .05 was considered statistically significant. For the comparison of abnormal HVIN prevalence between each groups (VN vs SSNHL-V, VN vs RHS-V, and SSNHL-V vs RHS-V), P < .017 was considered statistically significant.
Results

VIN in Patients with VN, SSNHL-V, and RHS-V

Ninety-five of 104 patients with VN (91%, 13.8 ± 8.7/s), 24 of 27 patients with SSNHL-V (89%, 10.4 ± 8.2/s), and 16 of 17 patients with RHS-V (94%, 13.9 ± 11.4/s) showed abnormal VIN (Figure 1). The direction of the slow-phase eye movements was always toward the lesioned side, and the prevalence of an abnormal VIN was not significantly different among the 3 disease groups (P = .436 by chi-square test). SPVavr, which was calculated by averaging SPVs obtained from vibrating right and left mastoid bones, was used to evaluate the relationship between CP and VIN in patients with VN, SSNHL-V, and RHS-V. Caloric tests indicated that CP values were 58.7% ± 18.6%, 51.6% ± 19.4%, and 55.6% ± 23.8% in patients with VN, SSNHL-V, and RHS-V, respectively. CP was not significantly different among the 3 groups (P = .625). Linear regression was used to determine the relationship between CP and SPVavr of VIN. A plot of the SPVavr values of VIN against CP values is shown in Figure 2. Statistically significant, although weak, correlations were observed for all 3 disease groups (r² = 0.169, P < .001 for VN; r² = 0.395, P = .001 for SSNHL-V; r² = 0.315, P = .0024 for RHS-V). The intercepts/slopes of the linear regression equations fitting SPVavr of VIN as a function of CP were 1.628/0.202 (VN), −3.250/0.257 (SSNHL-V), and −8.093/0.364 (RHS-V) (Table 1).

HVIN in Patients with VN, SSNHL-V, and RHS-V

HVIN was abnormal in 53 of 104 patients with VN (51%), 6 of 27 patients with SSNHL-V (22%), and 10 of 17 patients with RHS-V (59%) (Table 2, Figure 1). The prevalence of abnormal HVIN was significantly different between patients with SSNHL-V and VN (P = .007) and between patients with SSNHL-V and RHS-V (P = .014). In contrast, those with VN and RHS-V did not show a significant difference in the prevalence of abnormal HVIN (P = .547). In patients with VN, HVIN beating toward the lesioned side (ipsilesional HVIN) occurred in 23 of 104 patients (22%), and HVIN beating toward the intact side (contralesional HVIN) occurred in 30 of 104 patients (29%). The SPVs of HVIN for the ipsilesional and contralesional HVIN were 41 ± 51/s (5-168/s) and 7 ± 4/s (4-19/s), respectively. These were significantly different from each other (P = .005). The CP values for the ipsilesional and contralesional HVIN groups were 61% ± 16% (26%-86%) and 65% ± 18% (30%-100%), respectively. These were not significantly different from each other (P = .429). In patients with SSNHL-V, ipsilesional HVIN occurred in 3 of 27 patients (11%), whose SPVs of HVIN and CP were 24 ± 21/s (7-47/s) and 39% ± 16% (23%-55%), respectively. Contralesional HVIN was observed in 3 of 27 patients (11%), whose SPVs of HVIN and CP were 8 ± 4/s (5-12/s) and 51% ± 13% (36%-59%), respectively. In RHS-V, ipsilesional HVIN was observed in 4 of 17 patients (24%), and contralesional HVIN was observed in 6 of 17 patients (35%). The SPVs of HVIN for the ipsilesional and contralesional HVIN were 11 ± 5/s (5-16/s) and 7 ± 4/s (4-15/s), respectively. The CP values for the ipsilesional and contralesional HVIN groups were 60% ± 31% (27%-95%) and 67% ± 18% (44%-88%), respectively.

Discussion

Our results show that HVIN is significantly more common in patients with VN and RHS-V than in those with SSNHL-V, although no significant differences were observed in the prevalence of VIN or caloric CP among these diseases.

VIN is known as a sensitive and simple clinical test for detecting peripheral vestibular asymmetry. It was reported that vestibular cell receptors are excited by vibration and evidence of vestibular receptor cell activation by oscillating mechanical stimulus delivered to the hair bundle was demonstrated. Mechanical deflection of hair bundles of the vestibular hair cell showed a sigmoidal response curve. Deflection of the hair bundles toward the kinocilium.
activated the hair cell without complete saturation, and deflection away from the kinocilium inactivated the hair cell with abrupt saturation, which would result in an excitatory net effect. However, it is not yet clearly determined how the vestibular system is stimulated to generate VIN by vibration. It has been presumed that skull vibration elicits a pressure wave in the cerebrospinal fluids, and the pressure wave is propagated into the inner ear fluids via the cochlear and vestibular aqueducts and internal auditory canal, which has been suggested as a mechanism that may mediate vibratory excitation of the vestibular receptors. The present study showed that the prevalence of VIN was not significantly different among patients with VN, SSNHL-V, and RHS-V and also that the direction of SPV was consistently toward the lesioned side. Moreover, regardless of the diagnosis among patients with significant VIN, the SPV of VIN was increased as a function of CP as observed in a previous study. This suggests that the vibration test, like the caloric test, can probe imbalances of the lateral semicircular canal/superior vestibular nerve function in patients with peripheral vestibulopathy of various disease entities at acute stages.

The presence of HVIN has been reported to be determined by the alteration in neuronal excitability in the vestibular system. Partial demyelination of the vestibular nerve was suggested as a mechanism for ipsilesional HVIN. An increase in cerebrospinal fluid pH by hyperventilation results in a reduction in extracellular ionized Ca\(^{2+}\) levels, which leads to improvement of axonal conduction in partially demyelinated nerve fibers. The mechanism for contralesional HVIN was explained as the disruption of the central static compensation, which had restored resting neuronal excitability in the vestibular nucleus after peripheral vestibular deficit. Cerebral vasoconstriction and a leftward shift of the hemoglobin oxygen dissociation curve resulting from hyperventilation may in some way compromise the vestibular compensatory mechanism. The determination of the direction of HVIN will depend on the relative intensity between recovery of conduction block of the partially demyelinated vestibular nerve (ipsilesional HVIN) and impairment of central compensation (contralesional HVIN) by hyperventilation. In patients with vestibular schwannoma, both ipsilesional and contralesional HVINs were observed preoperatively, whereas only contralesional HVIN was observed postoperatively, possibly due to an extensive degree of damage to the vestibular nerve. Similarly, while both ipsilesional and contralesional HVINs were elicited at an acute stage of VN, only contralesional HVIN was observed at a follow-up stage (2 months) of VN, presumably due to recovery of demyelination at this stage. HVIN has been reported to be more common in retrocochlear lesions than in end organ diseases. In the present study, HVIN was significantly more common in patients with VN and RHS-V than in those with SSNHL-V.

Figure 2. Correlation between averaged values of slow-phase velocities (SPVs) of vibration-induced nystagmus (VIN) and the degree of canal paresis (CP) in the caloric test. Slow-phase velocity of VIN increases as a function of caloric CP in vestibular neuritis (VN) (A), sudden sensorineural hearing loss with vertigo (SSNHL-V) (B), and Ramsay Hunt syndrome with vertigo (RHS-V) (C).
is caused by the transmission of biochemical changes in the inner ear fluid from the cochlea to the vestibular organs. Radiological evidence for the pathologic condition within the inner ear in SSNHL-V has been demonstrated, and clinical findings suggesting end organ damage have been reported. In VN, the pathologic site is believed to lie within the vestibular nerve, and degeneration of the vestibular nerve with or without vestibular hair cell damage has been observed. In contrast, the lesioned site of RHS-V that is responsible for the vestibular deficit is still a subject of great controversy. Electrophysiological, histopathological, and radiological evidence suggests that the site of the vestibular deficit is located in the end organ, vestibular nerve, or both. Two patients with RHS-V showed high signals in the inner ear on precontrast 3D-FLAIR MRI, which suggested an abnormal elevation of blood vessel permeability. Another study showed that 11 of 12 RHS-V patients exhibited enhancement of the superior vestibular nerve within the internal auditory canal on MRI. By use of caloric testing and vestibular-evoked myogenic potentials by click sound and galvanic stimulation, the diversity of lesioned sites—including vestibular nerve and/or labyrinth—was suggested as an origin of vestibular symptoms in RHS-V.

The most interesting findings of the present study were that the prevalence of VIN, which is thought to be generated by the asymmetry of receptor cells in the vestibular end organ, was not significantly different among patients with VN, SSNHL-V, and RHS-V, whereas the prevalence of HVIN, which is known to originate from lesions in the vestibular nerve and/or central vestibular system, was significantly different between patients with SSNHL-V and VN or RHS-V. Thus, it is notable that RHS-V showed profiles of VIN and HVIN results similar to those of VN, even though most (16/17) patients with RHS-V, as observed in patients with SSNHL-V, also showed sensorineural hearing loss on the affected side. These findings suggest that the vestibular deficit in RHS-V patients, whose caloric CP values are 25% or more, is more attributable to lesions in the vestibular nerve than to those in the vestibular end organ. However, because the results of VIN and HVIN were obtained from the patients who showed caloric CP values of 25% or more, the results of VIN and HVIN may be limited. It is known that facial paralysis in RHS is caused by reactivation of the varicella-zoster virus, which was infected latently in the geniculate ganglion of the seventh cranial nerve. The facial nerve was reported to have a direct connection to the superior vestibular nerve within the internal auditory canal, and viral transmission through this connection can elicit inflammation.

### Table 1. Linear Regression of SPV of VIN on Caloric CP.

<table>
<thead>
<tr>
<th>Condition</th>
<th>SPV of VIN</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>P Value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>VN</td>
<td>CP</td>
<td>0.202</td>
<td>0.046</td>
<td>&lt;.001</td>
<td>0.110 to 0.294</td>
</tr>
<tr>
<td></td>
<td>Constant</td>
<td>1.628</td>
<td>2.916</td>
<td>.578</td>
<td>−4.163 to 7.419</td>
</tr>
<tr>
<td>SSNHL-V</td>
<td>CP</td>
<td>0.257</td>
<td>0.068</td>
<td>&lt;.001</td>
<td>0.117 to 0.398</td>
</tr>
<tr>
<td></td>
<td>Constant</td>
<td>−3.250</td>
<td>3.971</td>
<td>.422</td>
<td>−11.485 to 4.986</td>
</tr>
<tr>
<td>RHS-V</td>
<td>CP</td>
<td>0.364</td>
<td>0.143</td>
<td>.024</td>
<td>0.057 to 0.671</td>
</tr>
<tr>
<td></td>
<td>Constant</td>
<td>−8.093</td>
<td>9.092</td>
<td>.388</td>
<td>−27.593 to 11.407</td>
</tr>
</tbody>
</table>

### Table 2. Prevalence of HVIN in Patients with VN, SSNHL-V, and RHS-V.

<table>
<thead>
<tr>
<th>Condition</th>
<th>HVIN (+)</th>
<th>HVIN (−)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>VN</td>
<td>53 (51%)</td>
<td>51 (49%)</td>
<td>104 (100%)</td>
</tr>
<tr>
<td></td>
<td>Ipsilesional HVIN = 23 (22%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Contralesional HVIN = 30 (29%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSNHL-V</td>
<td>6 (22%)</td>
<td>21 (78%)</td>
<td>27 (100%)</td>
</tr>
<tr>
<td></td>
<td>Ipsilesional HVIN = 3 (11%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Contralesional HVIN = 3 (11%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RHS-V</td>
<td>10 (59%)</td>
<td>7 (41%)</td>
<td>17 (100%)</td>
</tr>
<tr>
<td></td>
<td>Ipsilesional HVIN = 4 (24%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Contralesional HVIN = 6 (35%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: HVIN, hyperventilation-induced nystagmus; RHS-V, Ramsay Hunt syndrome with vertigo; SSNHL-V, sudden sensorineural hearing loss with vertigo; VN, vestibular neuritis.

*ipsilesional HVIN was defined when the nystagmus beat toward the lesioned side, and contralesional HVIN indicates nystagmus beating toward the intact side. The prevalence of HVIN was significantly different between SSNHL-V and VN (P = .007, chi-square test) and between SSNHL-V and RHS-V (P = .014, chi-square test), whereas a significant difference in the incidence of HVIN was not observed between VN and RHS-V (P = .547, chi-square test).
of the superior vestibular nerve, resulting in abnormal caloric CP, VIN, or HVIN.

**Conclusion**

Considering that the findings of VIN and HVIN in RHS-V patients were more comparable to those in VN patients than those in SSNHL-V patients, it can be assumed that the vestibular deficit in patients with RHS-V is more likely attributable to a lesion in the vestibular nerve than to an inner ear abnormality. However, the findings of VIN and HVIN may not be applicable to all SSNHL or RHS patients because only patients exhibiting caloric CP of 25% or greater were included in the present study.

**Author Contributions**

Chang-Hee Kim, substantial contributions to the conception and design of the work, revising it critically for important intellectual content, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; Kyung-Hwa Jeong, acquisition of data, drafting the work, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; Sung Hwan Ahn, analysis of data, drafting the work, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; Dong Hyuk Shin, interpretation of data, drafting the work, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; Yong Won Kim, interpretation of data, drafting the work, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; Jung Eun Shin, acquisition of data, drafting the work, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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