

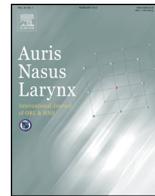


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## Vestibular neuritis: Involvement and long-term recovery of individual semicircular canals

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### ABSTRACT

**Objective:** In this retrospective study, the aim of the authors was to examine the frequency of involvement of the individual semicircular canals (SCCs) in vestibular neuritis (VN) and to assess the degree of long-term recovery. A secondary aim was to retrospectively determine the usefulness of a three-step bedside oculomotor test (the HINTS-test) for the differential diagnosis of peripheral VN.

**Methods:** 44 cases were evaluated during the acute phase and approximately two months later. The gain of the vestibuloocular reflex was determined using video-head-impulse test, carried out using Otometrics ICS Impulse Otosuite Vestibular V 1.2.

**Results:** In 19 cases (43%), a typical, so called “superior” VN could be diagnosed; in 17 cases (38%), all three SCCs were involved; in 4 cases, an isolated inferior canal involvement was seen; and in another 4 cases, a slight, isolated horizontal canal involvement was registered. Slight, isolated horizontal canal vestibular neuritis causing acute vestibular syndrome has not yet been reported in the literature. A three-step bedside oculomotor examination, the HINTS-test (head-impulse test, examination of gaze evoked nystagmus, and test of skew-deviation), suggested peripheral involvement in all cases with superior pattern VN and in cases when all three SCC were involved. It indicated ‘stroke’ in cases with inferior pattern and in the cases with isolated involvement of the horizontal canal. At follow-up, the horizontal canal function normalized in 55%, the anterior canal in 38%, and the inferior in 38%. When all cases were pooled, 14 patients recovered completely. In cases with severe initial decrease of gain in the horizontal canal (initial value less than 0.5), the canals had a 50 per cent chance to recover significantly.

**Conclusion:** In vestibular neuritis, in cases with severe decrease of gain in the horizontal canal (initial value less than 0.5), the canal has a 50 per cent chance to recover significantly. The vertical canals have worse prognosis, and especially the inferior canals seldom improve. Slight, isolated horizontal canal vestibular neuritis may cause acute vestibular syndrome, most probably by the same mechanism as full-blown vestibular neuritis. In these cases, the three-step bedside oculomotor test may indicate cerebellar stroke (may be false positive).

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## 1. Introduction

Acute vestibular syndrome (AVS; acute dizziness, accompanied by nausea/vomitus, gait unsteadiness, nystagmus, and intolerance to head motion lasting >24 h) is most frequently caused by vestibular neuritis (VN) or ischemic stroke in the brainstem or cerebellum [1]. Posterior fossa strokes are potentially dangerous; therefore, an early diagnosis is imperative. Spontaneous nystagmus and bilaterally normal horizontal bedside head-impulse test constitutes a red flag concerning possible central vestibular lesion and is one of three dangerous oculomotor signs (normal bedside head-impulse test in the horizontal plane, direction-changing nystagmus, and skew deviation), which were suggested by Kattah et al. to differentiate between peripheral and central causes of AVS (HINTS-test: (head-impulse test, examination of gaze evoked nystagmus, and test of skew-deviation)) [2]. Since the advent of three-dimensional video-head-impulse test (vHIT), it is possible to assess individual semicircular canals, even in the acute phase of a VN. It has been known that in VN sometimes only the superior part of the vestibular labyrinth (the anterior and horizontal semicircular canal) is involved; in other cases, there is an isolated impairment of the inferior canal [3–5]. Not surprisingly, the horizontal HIT, which can be carried out at the bedside, may suggest central pathology in peripheral vestibular neuritis when only the posterior (inferior) semicircular is involved. The HINTS-test was shown to identify stroke with high sensitivity (100%) and specificity (96%) in patients with acute vestibular syndrome [1]. The value of this new diagnostic algorithm is currently being assessed in the literature; it may be therefore interesting how often HINTS turns out to be false positive indicating stroke in cases with peripheral involvement.

After the acute phase of VN patients gets invariably better and most of them become symptom free with central compensation, semicircular canal function, however, does not always recover for stimuli with high acceleration. In the literature, quantitative data of gain values collected during head-impulse testing are scarce. Schmid-Priscoveanu et al. compared results of quantitative head-impulse testing using search coils with eye-movement responses to caloric irrigation in patients with unilateral vestibular hypofunction after vestibular neuritis. The authors found that the low-frequency function of the labyrinths often recovered to be symmetrical; however, the high-acceleration head-impulse test results showed less frequent improvement [6]. A few years later, the same group also stated that the ocular response to ipsilesional rotations in patients after VN frequently improves over time, possibly because of ipsilesional recovery [7]. Magliulo et al. [8] published qualitative data concerning involvement and recovery of individual semicircular canals. The incidence of superior and inferior branch neuritis was 55%, and superior branch involvement was found in 40%, and in 5%, inferior branch involvement was found.

Our first goal in this retrospective study was to examine the frequency of involvement of the individual semicircular canals in vestibular neuritis and the degree of long-term improvement. We asked how often a functionally useful recovery happens concerning stimuli with high frequency/high acceleration and if

there is a correlation with the degree of the initial function loss. A secondary aim was to retrospectively determine the usefulness of a three-step bedside oculomotor test (the HINTS-test) for the differential diagnosis of peripheral VN. Therefore, we also assessed the frequency of false-positive HINTS in the different types of VN.

## 2. Patients and methods

In this retrospective study, the data of cases with the diagnosis “peripheral vestibular neuritis” were collected at the Department of Otolaryngology (Karl Landsteiner University Hospital Krems, Krems an der Donau, Austria) from the period between August 2012 and May 2015. Diagnostic tools included documenting the acute signs of peripheral harmonic vestibular signs and symptoms (oculomotor and spinocerebellar signs), video-head-impulse testing, and audiometry.

Before data collection, permission has been obtained from the Ethical Commission of Lower Austria (GS1-EK-4/318-2015). Cases were included if admission occurred after 1st August 2012, and all follow-up examinations were completed before 30th May 2015.

Inclusion criteria were as follows: adults over 18 years of age; final diagnosis: “peripheral vestibular neuritis”; results were available of video-head-impulse testing done in the first two days after the appearance of symptoms. Exclusion criteria were as follows: involvement of central vestibular structures at final diagnosis; missing results of follow-up examination. Therapy did not include steroids, because a relatively recent Cochrane review did not find sufficient evidence in favor of corticosteroids [9]. Instead, it only consisted of supportive treatment, and in some cases of infusion therapy (vitamin B1, B12 and pentoxifyllin).

## 3. Examination methods

In their systematic review, Tarnutzer et al. [1] discussed the limitation of the caloric test in the acute care setting. Apparently, since the caloric reaction may indicate decreased peripheral function in stroke of the anterior inferior cerebellar artery territory, it may not help the topodiagnosis between central or peripheral acute vestibular syndrome. Therefore, when adapting the HINTS-test, audiometry and video-head-impulse testing as test battery for acutely diagnosing vestibular neuritis in the emergency care unit, we did not include the results of caloric test or vestibular evoked potential measurements as diagnostic criteria. This may be a new way of diagnosing vestibular neuritis reflecting the new topodiagnostic principles and the importance of differentiating between cerebellar stroke and purely peripheral vestibular neuritis in the emergency care setting. The accuracy of the bedside method (based on the three-step oculomotor examination including bedside horizontal head-impulse test) is further enhanced by the high resolution of the three-dimensional video-head-impulse test, which shows the involvement of individual semicircular canals.

All examinations, except audiometry, were done by the same experienced examiner (B.B.). During data acquisition, the

following parameters were collected retrospectively: date of admission and of the first measurements, age and sex of the patients, direction of the spontaneous nystagmus, results of HINTS-test (patients were included regardless of the HINTS-test results), and gain of the different semicircular canals as measured by video-head-impulse test at approximately 160°/s head velocity on the day of admission and at the follow-up examination, which occurred approximately after two months. The three-step clinical HINTS-test was done as recommended in [2]. Briefly, it consisted of horizontal bedside HIT-test + test of skew-deviation + gaze evoked nystagmus. It was considered to suggest a central vestibular cause if the head-impulse test was bilaterally normal and/or in the presence of skew deviation and/or gaze evoked nystagmus as opposed to the ‘peripheral HINTS’ pattern with a pathological HIT to the side of the nystagmus slow-phase and no skew-deviation and no gaze evoked nystagmus. vHIT-Test was carried out using Otometrics ICS Impulse Otosuite Vestibular V 1.2. Gain values were determined using the average value of software-calculated individual gain values of separate impulses with a velocity between 140°/s and 180°/s. The result of the vHIT was considered pathological in the case of a horizontal canal if the gain was under 0.8. In the case of the vertical canals, the established gain-norm in our laboratory is over 0.7; under this value, the vertical canal function is considered pathological. Apart from gain values, visual inspection of the time versus eye/head velocity panels was done in order to find and exclude goggle-slip artifacts. The presence of corrective saccades in the time period up to 200 ms after the impulse was considered obligatory for the validation of decreased gain values.

Audiometry was done using Interacoustics Equinox Affinity Suite AC440. Final diagnosis was complemented by follow-up radiological examinations (MRI of the head or contrasted cranial CT) in all cases except in cases with a well-defined superior VN with ‘peripheral HINTS’ pattern. That means that all cases were evaluated with only one semicircular canal (SCC) involvement and when all three semicircular canals were involved. Statistics were done using Graphpad Prism<sup>®</sup> Software.

## 4. Results

We identified 44 cases with acute peripheral VN treated at our department between August 2012 and May 2015; 22 males and 22 females were involved. Average age was 51 years (min.: 25, max.: 78, SD = ±14.3 years). In one case, diabetes mellitus (type 1) was noted. Average follow-up occurred after a 67 days (min.: 30, max.: 376, SD = ±61 days). Average time until data acquisition was 329 days (SD = ±297 days). Until data acquisition, no recurrence occurred. In 3 cases, VN on the same side had already occurred years before. In two cases, in which all three SCCs were involved, patients had long-term complaints corresponding to chronic vestibular insufficiency (instability in darkness, oscillopsia). In two cases, inferior canalolithiasis (benign paroxysmal vertigo) could be diagnosed and treated at follow-up. In three cases (one with three SCC involvement and two with isolated inferior SCC neuritis), acute hearing loss accompanied the vertigo in the acute phase and it did not improve at follow-up.

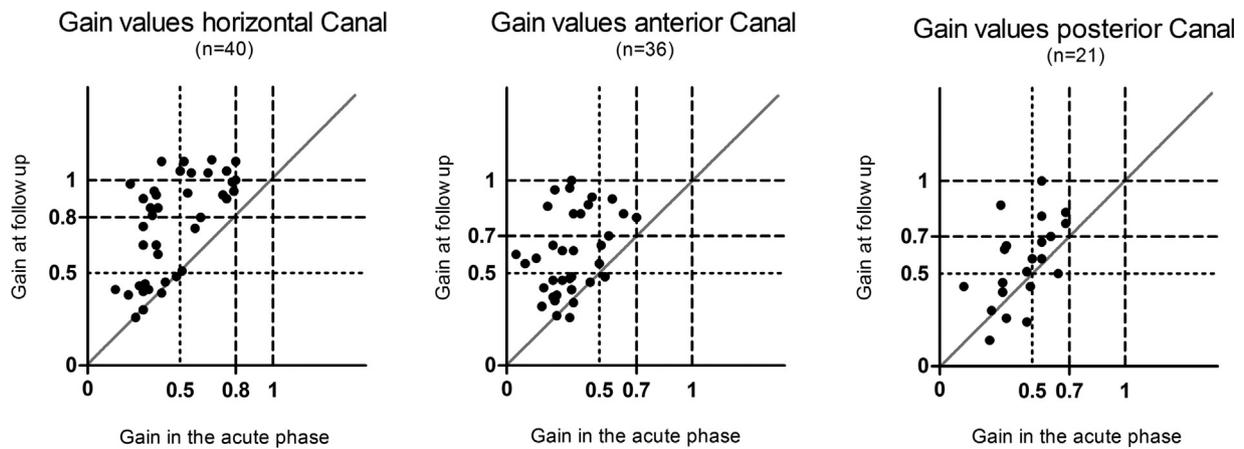
### 4.1. Measurements in the acute phase

We diagnosed VN on left side in 24 cases, and on the right in 20 cases. In 19 cases (43%), a typical, well-defined, so called “superior” VN could be diagnosed (involvement of the anterior and lateral SCCs); in 17 cases, all three SCCs were involved (38%); in 4 cases, an isolated inferior canal involvement was seen; and in another 4 cases, a slight horizontal canal involvement could be registered. HINTS suggested peripheral involvement in all cases with superior pattern VN and in cases when all three SCC were involved. It indicated stroke (it was false positive) in all 4 cases of VN with inferior pattern and in the 4 cases with isolated involvement of the horizontal canal (in sum in 8 cases out of 44 = 9%). In all of these 8 cases, the HINTS was false positive (indicated “stroke”), because, although there was a distinct spontaneous nystagmus, the clinical, bedside head-impulse test gave bilaterally normal results. Gaze evoked nystagmus and/or skew deviation were not noted. This pattern has been described in isolated smaller infarctions involving the territory of the medial posterior inferior cerebellar artery [10]. In the 4 cases with inferior canal involvement, the slight spontaneous nystagmus beats contained torsional components and were directed contralaterally, obliquely sideways and down (which is to be anticipated when a relative preponderance of the spontaneous activity arising in the corresponding canal pair, in the contralateral superior canal occurs, corresponding to the ipsilateral decreased activity in the inferior canal). In the 4 cases with a slight horizontal canal involvement, the spontaneous nystagmus was beating purely horizontally with a contralateral fast phase; it obeyed Alexander’s law and was enhanced by horizontal head shaking.

On the contralateral side, all canals were in the normal range in the acute phase (average gain ± SD, horizontal canal:  $1.0 \pm 0.17$ ; anterior canal:  $0.8 \pm 0.16$ ; inferior canal:  $0.78 \pm 0.17$ ).

### 4.2. Follow-up measurements

At follow-up, no worsening of gain in cases of normal, not involved canals occurred on the involved side. On the contralateral (normal) side, all canals were in the normal range also at the follow-up measurement (average gain ± SD, horizontal canal:  $0.98 \pm 0.14$ ; anterior canal:  $0.83 \pm 0.16$ ; inferior canal:  $0.82 \pm 0.16$ ). On the involved side, the horizontal canal function normalized in 22 cases (out of 40; 55%), the anterior canal in 14 cases (out of 36; 38%) and the inferior in 8 cases (out of 21; 38%). None of the cases improved in which in the acute phase an isolated inferior SCC involvement had occurred; but in all cases, a complete recovery was observed when in the acute phase a slight, isolated horizontal canal function loss had been demonstrated. Out of 44 patients, 14 recovered completely (out of 44 = 31%), which means that all of their SCCs functioned normally at follow-up. In the 3 cases, when a VN on the same side had already occurred years before, all SCCs recovered completely. A quantitative analysis of the initial loss of gain versus gain at follow-up is shown in Fig. 1. At an arbitrary 0.5 gain, vertical

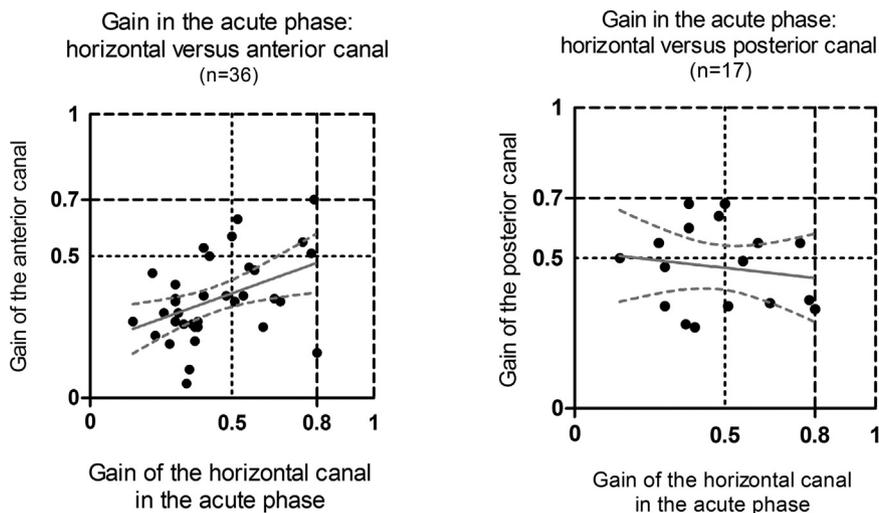


**Fig. 1.** Initial loss of gain of the involved canals versus gain at follow-up. Dashed lines show unity gain and the lower limit of the normal gain values. At 0.5 gain, additional vertical and horizontal dashed lines have been drawn to separate light versus severe gain decrease. Originating at zero, a  $x = y$  line separates regions with improvement (above the  $x = y$  line) from deterioration (below the line) at follow-up.

and horizontal lines have been drawn to separate light versus severe gain decrease. These lines help to notice that in the horizontal canal most cases with a slight gain decrease during acute phase recovered to be normal at follow-up. Also, there are no points below the  $x = y$  line, which means that the gain did not decrease at follow-up. In cases with severe decrease of gain (initial value less than 0.5), the canals had a 50 per cent chance to improve significantly. These trends are similar but less pronounced in the anterior canals and even less distinctive in the inferior canals. Here, in several cases the gain deteriorated at follow-up. In Fig. 2, the initial gain decrease was correlated between the horizontal and vertical canals. While the initial gain decrease in the acute phase showed a significant correlation between the horizontal and anterior canals, no such correlation could be observed when correlating the horizontal and inferior canals.

### 5. Discussion

Quantitative data concerning initial decrease and improvement of individual SCC gain values measured using high-velocity/high-acceleration stimuli in peripheral VN are scarce in the literature because high-speed video-head-impulse testing became only recently available in the clinical practice. The majority of data concerning improvement after VN have been obtained using caloric stimulation. In the studies in which improvement of gain values has been assessed quantitatively, the gain values always improved to a varying extent and ipsilateral recovery depended on improving peripheral semi-circular canal function [6,7,11]. This was similar in our group of patients. When all cases were pooled, in 31% of all cases the patients recovered completely; this meant that all of their SCCs functioned normally at follow-up. Patients who had previous



**Fig. 2.** Comorbidity of semicircular canals. Left panel: correlation of initial gain values between the horizontal and anterior canals in the acute phase (linear regression line shown  $\pm$  95% confidence interval (dashed curves), slope  $0.36 \pm 0.12$ ;  $R^2 = 0.19$ ; significant deviation from zero,  $p = 0.008$ ; Spearman  $r = 0.39$ ; two-tailed  $p$  value = 0.018). Right panel: correlation of initial gain values between the horizontal and inferior canals in the acute phase (linear regression line shown  $\pm$  95% confidence interval (dashed curves), slope  $-0.11 \pm 0.19$ ; not significantly deviating from zero; Spearman  $r = -0.01$ ; no significant correlation).

VN in their history had a good prognosis. On the contralateral side, the gain of the VOR was normal even in the acute phase. In case of the horizontal canals no deterioration of gain could be observed at follow-up. In cases with severe decrease of gain (initial value less than 0.5), the canals had a 50 per cent chance to improve significantly. These trends were similar but less pronounced in the anterior canals and even less distinctive in the inferior canals. Here, in several cases, the gain deteriorated at follow-up.

There were no cases with isolated anterior canal involvement among our patients, which is not surprising since no such case has been documented in the literature. We found ‘total’ and ‘superior’ pattern approximately as frequent as other authors [8]. Apart from the more common ‘superior’ pattern (anterior and lateral SCC involvement) and three-SCC pattern, we observed 4 cases with an isolated inferior canal involvement, and in another 4 cases, a slight horizontal canal involvement could be registered. The possibility of isolated inferior branch VN has been first suggested by Fetter and Dichgans [12] and since then it has been accepted as a less common but nevertheless clinically significant variety of VN [4,13]. We have not found any description of isolated horizontal canal VN in the literature. In the cases with isolated horizontal and inferior SCC involvement, the video-HIT examination was essential in making the diagnosis, since the three-step bedside oculomotor examination (HINTS-test) suggested stroke (it was false positive) and it would have been impossible to explain the complaints without exact gain values. In our material, this meant 8 cases out of 44 patients with VN (9%). In our view, the VN involving the isolated horizontal canal is a clinically important entity, since it may be as frequent as the isolated inferior pattern. Also, it may be missed by bedside HINTS-test although the patients exhibit strong imbalance and spontaneous nystagmus in the acute phase.

It has been suggested that there may be anatomical differences, which may make the superior vestibular nerve more susceptible to entrapment and ischemia, because the lateral bony channel of the superior vestibular nerve is seven times longer than the inferior vestibular and more than three times longer than the singular channel [14,15]. Interestingly, the fact that the anterior and horizontal SCC canals are innervated by superior branch of the vestibular nerve and the inferior branch is separated from them could be demonstrated in our material using the gain values in the acute phase: correlation could be shown between gain decrease in the anterior and horizontal canals but no such correlation could be demonstrated between the horizontal and inferior SCCs. When comparing recovery, there was a tendency for the vertical canals to recover less well: the horizontal canal function normalized in 55% and the vertical canals in only 38%. In some of the inferior canals, the function deteriorated at follow-up, which was not the case with the horizontal or anterior canals. Out of 4 cases with isolated inferior SCC involvement, none normalized at the follow-up. Currently, it is not clear why inferior SCC involvement might have a worse prognosis. It might be speculated that the shorter and broader bony canal of the inferior vestibular nerve allows for less entrapment and for better residual blood microcirculation during early phases of

the infection. The herpes viruses (which have been implicated in the pathogenesis of VN [16]) could therefore spread more easily to the vestibular end organ and to the cupula, making irreversible hair cell damage more possible.

In three cases (the inferior SCC was always involved), acute hearing loss accompanied the vertigo in the acute phase and it did not improve at follow-up. This latter phenomenon, inferior neuritis with accompanied hearing loss, has been observed by other authors [4,13].

## 6. Conclusions

The new findings of this study might be summarized as follows: In vestibular neuritis, in cases with severe decrease of gain in the horizontal canal (initial value less than 0.5), the canal has a 50 per cent chance to improve significantly. The vertical canals have worse prognosis, and especially the inferior canals seldom recover. Slight, isolated horizontal canal vestibular neuritis may cause acute vestibular syndrome, most probably by the same mechanism as full-blown vestibular neuritis. In these cases, the three-step bedside oculomotor test may indicate cerebellar stroke (may be false positive).

## Conflict of interest statement

The authors report no conflict of interest.

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