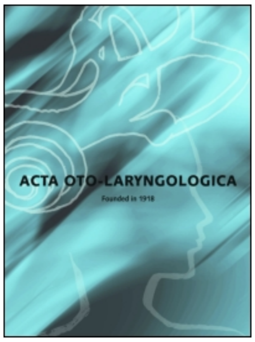

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RESEARCH ARTICLE

The characteristics of vHIT gain and PR score in peripheral vestibular disorders

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ABSTRACT
Background: Clinical application of vHIT is limited due to a lack of interpretation of vHIT gain and saccades.
Objectives: This research focuses on comparing common vertigo diseases on vHIT gain and saccade divergence(PR score).
Material and Methods: We retrospectively reviewed 165 patients who have one definite diagnosis, good data quality, and can be read by MATLAB software. All patients were grouped into unilateral vestibular dysfunction (UVD), Meniere's disease (MD), vestibular migraine (VM), Ramsay Hunt Syndrome (RHS), bilateral vestibular hypofunction (BVH), benign paroxysmal positional vertigo (BPPV), and acoustic neuroma (AN). PR score was calculated by an open-source software HitCal.
Results: The saccade detection rate is higher than the abnormal vHIT gain on UVD, MD, VM, RHS, BVH and BPPV. PR score combined with vHIT gain could separate the affected side in UVD and RHS. In the MD group, both vHIT gain and PR score have inconspicuous performance. We also found that different compensation levels and hearing loss status affect results.
Conclusions and Significance: vHIT gain combined with PR score enables a proper distinction among common vertigo diseases. PR score is more sensitive than the gain value on evaluating the physiological situation, vestibular compensation and disease progression.

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KEYWORDS
PR score; vHIT; Unilateral vestibular dysfunction; Meniere's disease

Introduction

Functional testing of the vestibular system is the basis of correct diagnosis, which will lead to proper therapy. Video head impulse test (vHIT), as a fast, non-invasive and quantitative assessment of all six semicircular canals, became widely employed in worldwide clinics. Together with the caloric test, otolith test, rotatory chair, vHIT provides a comprehensive vestibular function evaluation for patients with dizziness, vertigo or central system diseases.

Reduced Vestibular ocular reflex (VOR) gain and evident catch-up saccades are the two pathological signs in vHIT. Clinically, it seems that VOR gain is more commonly used than the saccades because of its simplicity, metrizability, and interpretability. However, interpretation of these VOR parameters has been under dispute. The normal range of VOR gain is not closer to consensus. Nicolas et al. suggested that the standard value of VOR gain should be greater than 0.6 [1], Hamish et al. proposed that 0.7 would be more accurate [2], and Isaac et al. argued that 0.8 should be the criterion [3]. Besides, physicians realized that the usability of VOR gain could be hampered by several pitfalls, such as slippage, calibration problems, and noise [4,5]. Therefore the clinical application of vHIT is limited, such as Meniere's disease(MD) can be considered normal in some research [6], while vHIT in MD patients can be abnormal in other's view [7].

Saccades were habitually described as overt and covert saccades based on the presence of their occurrence time [8]. Clinically, it is hard to explain these two kinds to patients for two reasons. 1) The final results were usually presented as an accumulative graph, which is hard to identify separately. 2) The combination of two kinds, which frequently appears, is also an essential sign of disease progression. Considering those two factors, the degree of saccades dispersion seems to be a relatively objective interpretation method. An open-source software named HitCal is a useful tool to measure the divergence between each saccade [9].

This present study attempted to compare PR score, calculated by the HitCal software, and vHIT gain in typical vertigo patients to add our understanding to evaluation about vestibular damage and compensation.

Materials and methods

Subjects

We retrospectively analyzed 386 patients admitted to the vertigo clinic at the Chinese PLA General Hospital from

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December 2019 to May 2020. Two authors (ZMW and LLR) carefully reviewed patients' information, including the history, medical records, imaging results, neuro-otological examination, audiology, and vestibular function tests. Acoustic neuroma (AN) were radiologically diagnosed and went through vHIT before surgery. MD was diagnosed according to the AAO-NHS criteria [10]. Vestibular migraine (VM) patients were identified according to the Barany Society diagnostic criteria [11]. The diagnosis of benign paroxysmal positional vertigo (BPPV) is based on the Barany Society 2015 diagnostic criteria [12]. Bilateral vestibular hypofunction (BVH) is diagnosed according to the Barany Society 2017 diagnostic criteria [13]. Ramsay-Hunt syndrome (RHS) with vertigo is diagnosed with an ipsilateral herpetic eruption on the auricle and external ear canal, facial palsy, and vertigo. The diagnosis of unilateral vestibular dysfunction(UVD) was based on the history of acute sustained vertigo or imbalance, abnormal results in the caloric test (unilateral weakness >25%) and no additional central lesion signs.

This study was approved by the ethical committee of the Chinese PLA General Hospital. Data concerning patients' age, sex, results of horizontal vHIT, canal paresis in the caloric test, pure-tone audiometry was collected. All those tests were performed on the same day. This study focuses on vHIT characters on certain peripheral vestibular disorders. We excluded 149 patients who have two or more diagnoses (such as a combination of UVD and BPPV, which may contain two characters on both groups). All vHIT results were carefully reviewed by a sophisticated medical technician who removed the bad quality results of slippage, eye blink, lousy calibration, lack of attention and pulses less than ten on each side ($N = 40$). For saccade analysis in HitCal, those data which could not be imported into MATLAB were also deleted from our list ($N = 32$). All data were grouped into UVD, MD, VM, RHS, BVH, BPPV and AN by the diagnoses, and their demographic characteristics can be seen in Table 1.

We further investigated the appearance of the vHIT features on evaluating vestibular compensation. Forty-five patients in the UVD group were subdivided into three groups by their clinical signs. Spontaneous nystagmus, head-shaking nystagmus were recorded by a video-oculography system (VO425, Interacoustics, Denmark), and postural asymmetries and imbalance, movement-induced visual instability and disturbance were collected by a written questionnaire. (1) Static deficits: 11 patients with positive spontaneous nystagmus, and complaints about postural imbalance. (2) Dynamic deficits: 25 patients with negative spontaneous nystagmus, and one of the following conditions: positive head-shaking nystagmus, complained postural imbalance, and oscillopsia. (3) Fully compensated: 9 patients without results and complaints about the postural and visual disturbance.

Fifty-three MD patients were subdivided into four groups regarding their four-tone average of the pure-tone thresholds at 0.5,1,2, and 3 kHz: mild (≤25 dB, $N = 15$), moderate (26-40 dB, $N = 23$), severe (41–70 dB, $N = 13$) and profound (>70dB, $N = 2$) [10]. Besides audiograms, visual and postural disturbances were also collected by the same video-oculography system and questionnaire. The subgroups on each hearing loss degree were divided based on the condition of visual or postural disturbance.

Table 1. Demographic characteristics.

Diseases	Age	Female/male
UVD	49.2 ± 13.2	21/24
RHS	46.6 ± 15.3	3/7
BVH	58.1 ± 14.0	11/3
AN	45.0 ± 21.3	1/4
BPPV	49.0 ± 15.0	19/8
VM	41.5 ± 9.1	6/5
MD	51.9 ± 14.0	25/28
Total	49.9 ± 14.5	86/79

PR score

All vHIT tests were performed with Otometrics (ICS Impulse, Denmark) by one sophisticated technician and were stored in XML (eXtensible Markup Language) format for further analysis by MATLAB (R2018 a, MathWorks, Natick, MA). We utilized only horizontal vHIT because the results of vertical vHIT were less reliable. Saccades clustering was analyzed by an open-source software HitCal, in which saccades can be classified into normal, scattered and gathered by PR score.

The PR score calculating method are as follows: (1) the time appearance of each group of saccades were recorded and listed as first, second, third and fourth saccades. All saccades have a minimum velocity of 65°/s. 2) Coefficient of variation (CV) of peaks in each group was calculated and marked as CV1, CV2, CV3 and CV4 by their appearance time. CV = (standard deviation/mean) * 100 = $(SD/\overline{X}) * 100$. Multiplying the coefficient by 100 is an optional step to get a percentage. 3) Global PR score = $2.5*(0.8*CV1 + 0.2*CV2)$ [9]. The range of PR value is from 0 (maximum gathered, all saccades have the same appearance time) to 100 (maximum scattered) as authors described before (different divergence levels were shown in Figure 1). In clinical application, no situation of 0 could appear, thus for the convenience of visualization, we use number 0 represent the situation of no saccade appearance.

Data analysis and visualization

All of the statistical analyses were performed using IBM SPSS 20.0 (SPSS Inc., Chicago, IL, USA), and all variables were presented as the mean ± standard deviation. To compare the difference between different subgroups, we performed one-way ANOVA and independent t-test. P-value <0.05 was identified as statistically significant and was demonstrated in the following figures. Since we were concerned about each patient's feature, data visualization was introduced in this study. The primary purpose of visualization is to gain quick insight into the features of vHIT gain and PR score in different diseases. To understand the effect of vHIT

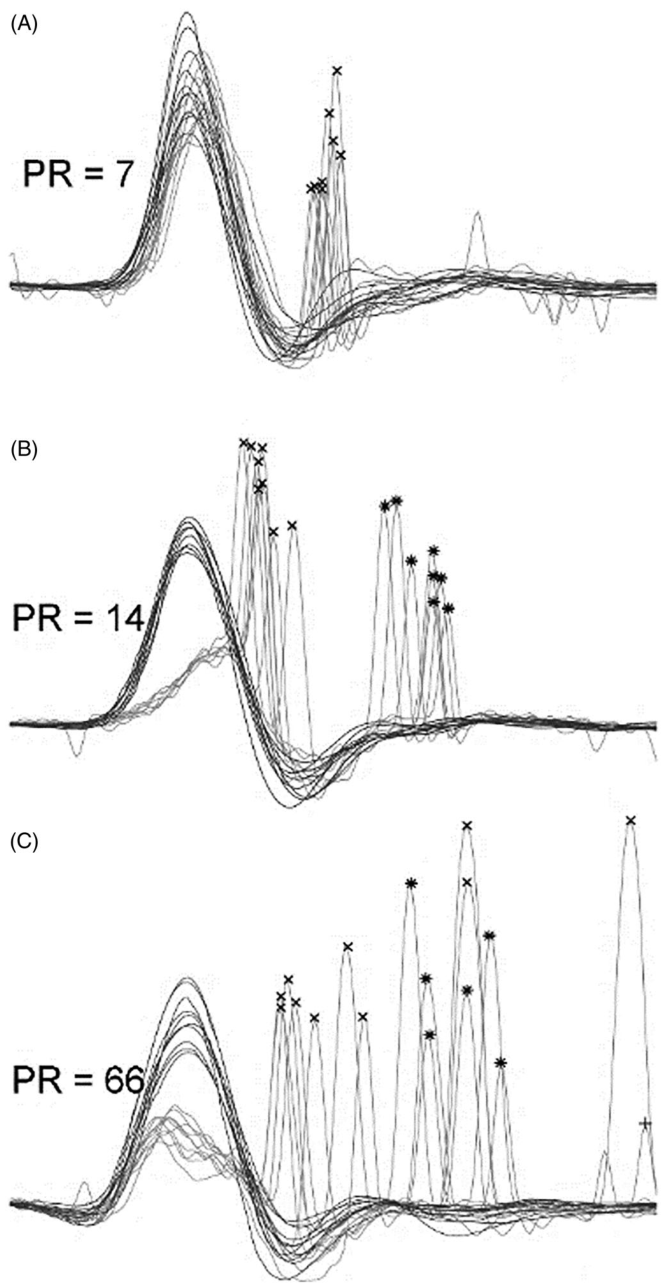

Figure 1. Different PR score represents a different clustering scale. (A) Patient #1: PR score equals to 7, only one saccade in each impulse. (B) Patient #2: PR score equals to 14, two saccades in each impulse, all are gathered together. (C) Patient #3: PR score equals to 66, two saccades in each impulse, but all are scattered.

gain and PR score on identifying the affected side, violin plots were used for data visualization. Violin plots can reveal the peaks, valleys, and bumps in the shape of distributions since they are valuable for identifying the clusters and comparing the occurrences. Figures were generated with Python 3.7 program.

Violin plots, swarm plots and box plots are visually combined in this research for better understanding. This combination not only carries information about individual values but also density distribution and statistical characteristics. In the violin plot, the higher densities (peaks) indicate more samples, and therefore more patients have this value. The lower densities (valleys) describes the boundaries of each category.

Table 2. vHIT parameter in common vertigo diseases.

Diseases	N	vHIT gain*	Abnormal vHIT gain rate*	Saccade rate*
UVD	45	0.74 ± 0.25	47%	91%
RHS	10	0.49 ± 0.16	90%	100%
BVH	14	0.54 ± 0.29	71%	79%
AN	5	0.80 ± 0.14	60%	60%
BPPV	27	0.98 ± 0.17	11%	41%
VM	11	0.93 ± 0.11	9%	18%
MD	53	0.95 ± 0.15	10%	60%

*vHIT gain is calculated by the average value by minimal vHIT gain on each side.
*Abnormal vHIT gain is defined as <0.8; the rate is calculated on both sides.
*Saccade rate is calculated by the PR score appearance rate on both sides.

Results

General characteristics of vHIT gain and PR score

The average vHIT Gain on UVD, RHS and BVH is lower than 0.8. The top 3 abnormal vHIT gain rate is 90% on RHS group, 71% on BVH group, and 60% on AN group. The top 3 saccade rate is 100% on the RHS group, 91% on UVD group and 79% on BVH group. Besides AN, saccade has a relatively higher detection rate than abnormal vHIT gain in each disease (Table 2).

The identification capability on vestibular lesion

This study compared the vHIT gain and PR score on the affected side and unaffected side from unilateral lesion diseases (UVD, RHS and MD). The vHIT gain scatters from 0.2 to 1.4 on the affected side and varies from 0.4 to 1.4 on the unaffected side, as shown in Figure 2. PR score diverges from 0 to 85 on both the affected side and the unaffected side (Figure 2). Comparatively, the positive saccade rate (non-zero PR score) is higher on the affected side. There is no apparent linear correlation between vHIT gain and PR score, as shown in Figure 2.

For UVD patients, the PR score and vHIT gain perform differently on the lesion side. As is shown in Figure 3(A), both vHIT gain and PR score on the affected side are significantly different from the unaffected side ($p < 0.001$). PR score on the affected side mostly centralized around 20 (Figure 3(B)). The saccade detection rate on the unaffected side is rare.

For RHS, the vHIT gain and PR score both have different performance on the affected and unaffected side ($p < 0.001$ on vHIT gain comparison, $p < 0.05$ on PR score comparison, shown in Figure 3(A)). Positive saccade rates are almost 100% on the affected side while very low on the unaffected.

For the MD group, the differences are not that clear on both sides ($p > 0.05$). Most vHIT gains are normal both on the affected and unaffected sides. The saccade appearance rate is half and half on each side—PR scores separate from

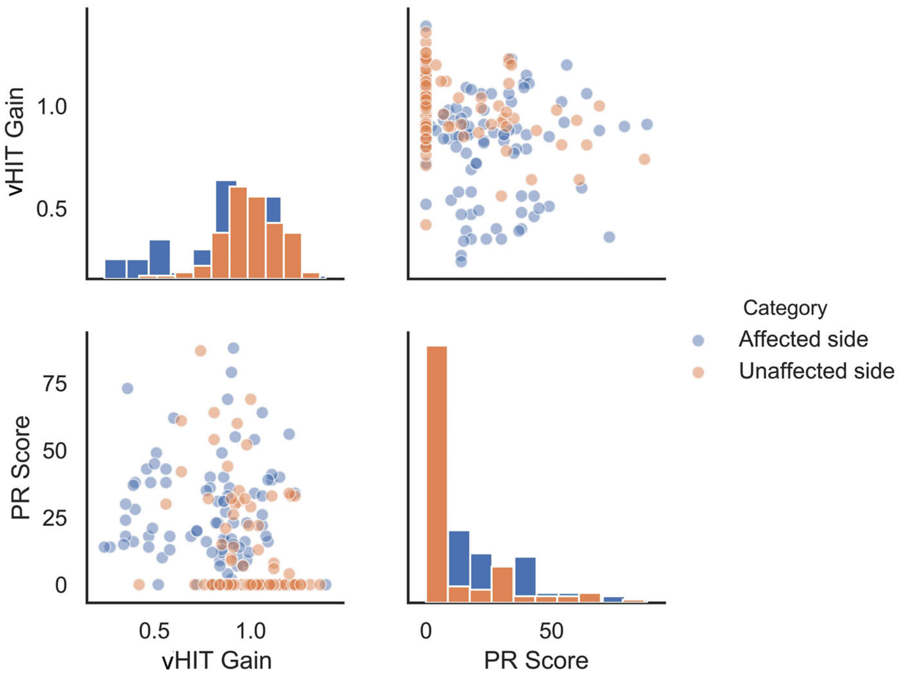

Figure 2. Histogram and pair plot of PR score and vHIT gain by the category of affected and unaffected in UVD, RHS, and MD. Compared to the unaffected side, the affected side has more positive PR score and lower vHIT Gain.

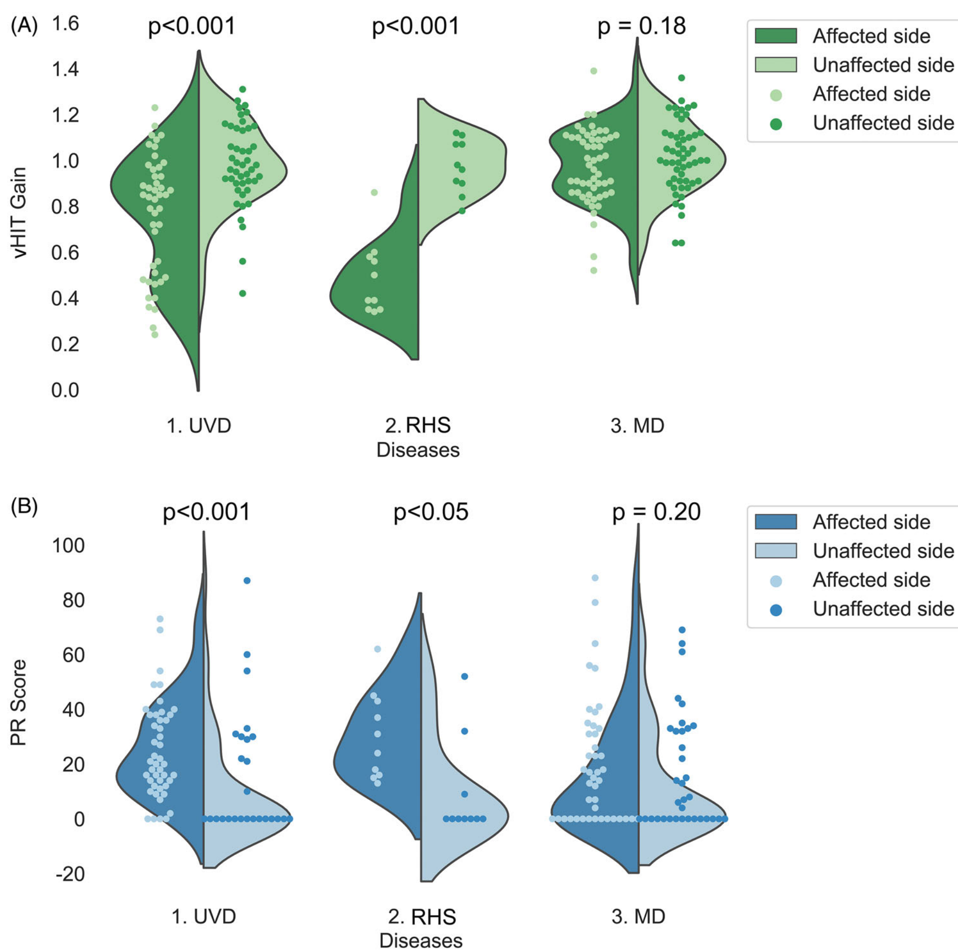

Figure 3. Violin plot and swarm plot reveals the levels and distributions of vHIT gain and PR score in UVD, RHS, and MD patients. Violin plots display the data distribution and its probability density. The inner swarm plotshows the distribution for each data. The left part for each violin plot represents the affected side in each disease; the right side of each violin plot represents the unaffected side in each disease. (A) vHIT gain. (B) PR score. The *t*-test result was present in each group.

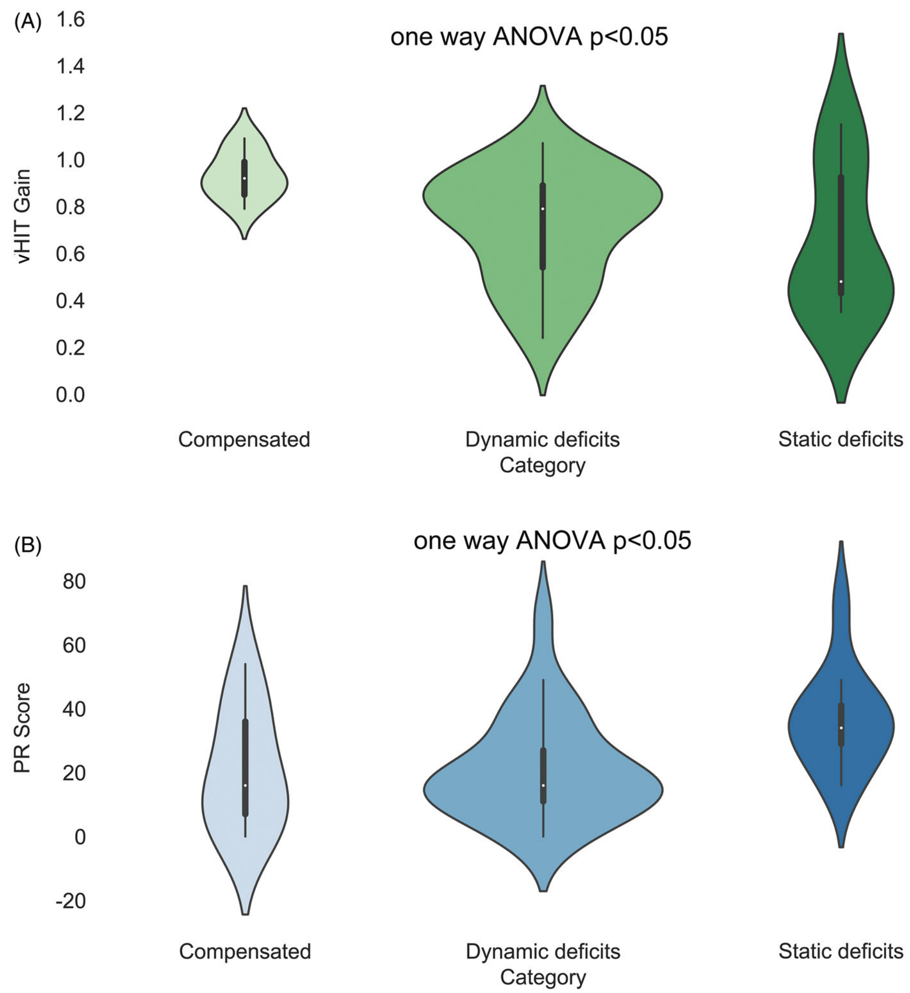

Figure 4. Violin plot compares the differences among three vestibular compensation status on UVD patients: compensated, dynamic deficits, and static deficits. (A) vHIT gain on the affected side. (B) PR score on the affected side. One-way ANOVA result was present on the top of each plot.

gathered to scattered (Figure 3(B)). The intra-class comparison on MD group will be further presented on 3.4.

Same disease may differ on vHIT features

For UVD patients, three compensation status shows statistically different vHIT gain and PR score (ANOVA test result $p < 0.05$). vHIT gain increased with compensation level, in which static deficits patients have the lowest gain (gathered around 0.4), and the next is the dynamic deficits, and the compensated group has the highest vHIT gain. While the PR score shows the opposite trend, in which the highest PR score (almost 40) exists in static deficits group, and the second-highest in the dynamic deficits patients and the last is compensated patients (Figure 4).

MD patients with definite visual or postural disturbance have a non-zero PR score and a relatively lower vHIT gain compared to the other side. Most vHIT gain on both sides is higher than 0.8. Although the positive saccade rate is higher on the positive visual or postural side, there is no statistical difference can be found (t-test $p > 0.5$). Besides, the one-way ANOVA test shows no distinct differences between different hearing loss degree groups, which can be found in Figure 5(B).

Discussion

This study evaluated vHIT gain and a new parameter PR score on different diseases UVD, RHS, BVH, AN, BPPV, VM, and MD. Compared to vHIT gain, PR score is a more sensitive and intuitive parameter on identifying the vestibular function. This result included the evaluation of identifying the affected side, evaluating the different function statuses, and vestibular compensation in vertigo diseases.

This study offers a comprehensive vHIT numerical evaluation related to all sorts of vertigo diseases, which are consistent with previous studies [8,14–16] – for example, Eduardo et al. [16] found that the vHIT gain on RHS patients was lower than vestibular neuritis, and the latter showed a higher recovery possibility. Eduardo also pointed out that the latency, velocity, and organization of saccades are relevant to vestibular compensation. Alexander et al. [14] reported a horizontal VOR gain deficit in 9% of VM patients, which is similar to our findings. In clinical applications, physicians always pursue higher detection rates and lower false alarm rates. For this purpose, the PR score seems to be a more useful indicator than vHIT gain to identify the damage status.

Saccade - feedback on vestibular rehabilitation - is essential to our understanding of vestibular plasticity. Saccades

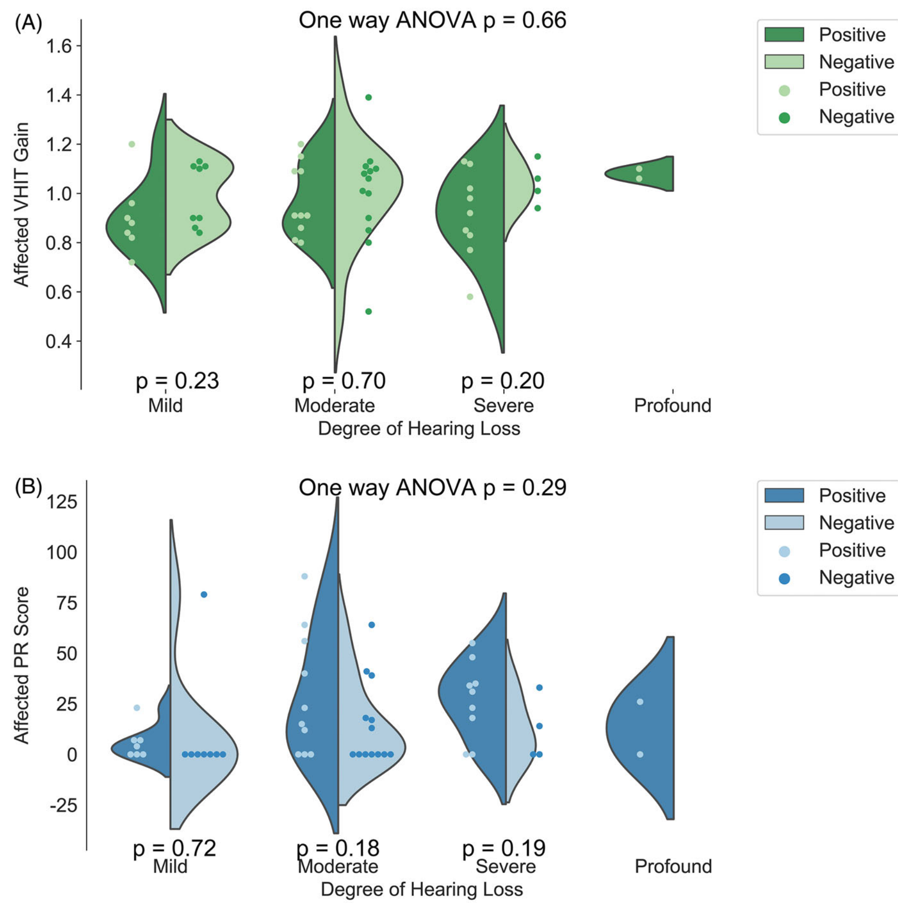

Figure 5. Violin plot compares the differences among four hearing loss degrees on MD patients: Mild, Moderate, Severe, Profound. The left part for each violin plot represents the positive visual or postural disturbance in each subgroup; the right side of each violin plot represents the negative visual or postural disturbance in each subgroup. (A) vHIT gain on the affected side. (B) PR score on the affected side. The t-test result was present in each group. One-way ANOVA result was present on the top of each plot.

decreased in frequency, amplitude, speed, and latency with gain recovery, suggesting that the brain learned to insert and refix saccades during recovery [17]. Former assessment of the recovery stages assumed that PR score changed from scattered to gathered was a hint of compensatory [18]. Our research related to different compensation status on MD and UVD patients supported this state. The gain and saccades attempt to change with different disease stages [16]. PR score, combined with vHIT gain, could provide a more comprehensive reference on compensation level, and may vary from patients. It can also explain why our study has disparity with other studies on abnormal vHIT rates, such as UVD, MD, BVH [7].

Although this research has provided a comprehensive evaluation of vHIT, other dimensions, including dynamic change after onset, should be focused on in our next study. The level of hearing impairment is related to saccade appearance on MD patients on our observation, but more samples should be included in our further work. Based on our observation, the cutoff of PR score on 55 [19] could not separate the compensation and decompensation level, as the author claimed, and therefore the standard should be evaluated in a larger sample. Besides, the situation of comorbidity, which is common in the clinic, will be discussed in our further work.

Conclusion

The present study results suggest that PR score is more sensitive than the vHIT gain on evaluating the physiological situation, vestibular compensation and disease progression. As the mathematical parameter represents the change of saccades from scattered to gathered, PR score also indicates different stages of recovery, which will add a new vestibular assessment method on the time scale.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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